Incidence of Brugada Electrocardiographic Pattern and Outcomes of These Patients After Intentional Tricyclic Antidepressant Ingestion

Vikhyat S. Bebarta, MD[a,*], Scott Phillips, MD[b], Aaron Eberhardt, MD[c], K.J. Calihan[d], Javier C. Waksman, MD, DABT[b], and Kennon Heard, MD[b]

Brugada syndrome is a genetic dysfunction of the myocardial sodium channel that leads to ventricular dysrhythmias. The electrocardiographic (ECG) pattern of Brugada syndrome is occasionally seen after tricyclic antidepressant (TCA) ingestion; however, the outcome and complication risk for these patients is not clear. The objective of our study was to describe the incidence of Brugada ECG pattern (BEP) and serious complications of these patients in a large case series of intentional TCA ingestions. We also compared the proportion of complications of patients with BEP versus those without BEP. We evaluated 402 TCA ingestions, of which 9 (2.3%) were associated with the development of BEP. We compared the adverse outcomes of all TCA ingestions versus TCA ingestions with BEP. A increase in the adverse outcomes in the BEP group was found: seizures (relative risk [RR] 4; 95% confidence interval [CI] 1.5 to 10.8), widened QRS (RR 4.8; 95% CI 1.8 to 12.9), and hypotension (RR 3.9; 95% CI 2.1 to 7.4). To reduce confounding ingestants, we also compared all patients with an isolated TCA ingestion versus those with BEP. A significant increase in adverse outcomes was again found with the BEP group: seizures (RR 3; 95% CI 1.1 to 8.6), widened QRS (RR 4.8; 95% CI 1.5 to 15.1), and hypotension (RR 3.4; 95% CI 1.9 to 22.3). No deaths or dysrhythmias were found in the BEP group. In conclusion, BEP after TCA ingestion is rare, and death or dysrhythmias did not occur. However, patients with BEP are likely at increased risk for TCA-induced complications. **(Am J Cardiol 2007;100:656–660)**

Brugada syndrome is associated with sudden death and is believed to be mediated by a genetic myocardial sodium channel dysfunction that leads to slow inward current.[1,2] Patients with Brugada syndrome have a characteristic electrocardiogram (ECG). Type 1 Brugada electrocardiographic pattern (BEP) is similar to a right bundle branch block with downsloping ST-segment elevation in leads V_1 to V_3 (Figure 1). Type IA antidysrhythmics can unmask BEP in some patients. Interestingly, overdose of medications with type IA antidysrhythmic effects, such as tricyclic antidepressants (TCAs), cocaine, and antipsychotic agents, has been associated with BEP.[3–8] However, the clinical significance of the BEP after ingestion of these medications has not been clearly defined. Goldgran-Toledano et al[3] suggested that the BEP may be a marker for death or poor outcome in a small series of patients with TCA and thioridazine overdose, although no difference in mortality was found between groups. The objective of our study was to describe the prevalence of BEP in a large case series of intentional TCA ingestions. In addition, we aimed to compare the incidence of adverse outcomes in the patients with BEP versus TCA ingestions without BEP.

Methods

This was a retrospective cohort study in which we reviewed previously collected medical records of patients with intentional TCA ingestions.[9,10] Patients were collected through a previous multicenter study of 9 participating medical centers.[9]

Patients were included in the study if they presented with a history of intentional antidepressant ingestion and had a measurable serum or urine TCA level. Patients were excluded if neither a measurable TCA level nor interpretable ECG was available for review. The patient records were collected from November 1990 to March 1993. The original study was approved by the institutional review board at participating hospitals and present study was approved at the coordinating center.

Trained reviewers used a standardized data collection form (DCF) to extract the data from the medical chart. Each reviewer used the DCF to collect the following information on each subject: age, gender, ethnicity, antidepressant(s) involved in the ingestion, and coingestants. The form specifically recorded the co-ingestion of the following drugs known to adversely affect myocardial sodium channels: quinine, propafenone, flecainide, chloroquine, procainamide, mexiletine, disopyramide, diphenhydramine, co-

[a]Division of Medical Toxicology, Department of Emergency Medicine, Wilford Hall Medical Center, San Antonio, Texas; [b]University of Colorado Health Sciences Center, Rocky Mountain Poison and Drug Center, Denver, Colorado; [c]Department of Emergency Medicine, Denver Health Medical Center, Denver, Colorado; and [d]Aurora Women's Care Clinic, Aurora, Colorado. Manuscript received December 14, 2006; revised manuscript received and accepted March 13, 2007.

*Corresponding author: Tel: 210-481-0040; fax: 702-442-7921.
E-mail address: vikbebarta@yahoo.com (V.S. Bebarta).

0002-9149/07/$ – see front matter
doi:10.1016/j.amjcard.2007.03.077

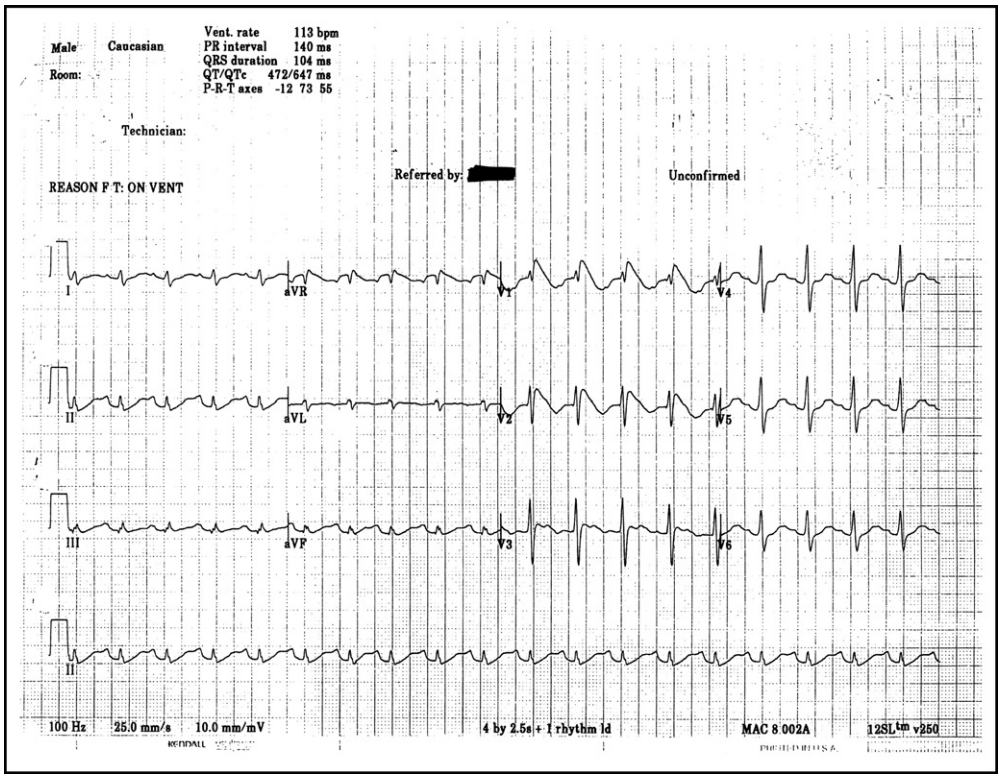

Figure 1. Example of BEP.

caine, amantadine, propoxyphene, propranolol, mesoridazine, carbamazepine, and phenytoin. Laboratory confirmation of TCA ingestion and detection of other ingestants was performed by serum or urine testing (or both) at a central laboratory (Analyitox, Englewood, Colorado) using ≥1 confirmatory method (thin-layer chromatography, gas chromatography, or high-performance liquid chromatography). The results were recorded on the DCF. Determination of coingestants was based on a combination of laboratory testing and history extracted from the medical record. If eitherdocumented a coingestant, the ingestant was recorded on the DCF.

All ECGs were reviewed by 1 abstractor and classified as BEP or non-BEP. BEP was defined as RSR′ (i.e., incomplete right bundle branch block pattern) in leads V_1 to V_3 with downsloping ST elevation and T-wave inversion. This pattern is referred to as type 1 and is the most common BEP.[2] A picture of the BEP was on the DCF. Patients were classified as having the BEP if any ECG in the record showed a BEP pattern. The primary author (V.S.B.), who was blinded to the clinical outcomes, reevaluated ECGs classified as BEP by the reviewers to ensure accuracy. The primary author and abstractors agreed on all BEP ECGs.

The reviewers were trained in data extraction on an initial sample of charts and were provided feedback. The reviewers reviewed ECGs with and without BEP before the initiation of the study to improve their diagnostic ability in identifying BEP. We also had ongoing meetings to answer questions and had continuous monitoring of the collected data. All definitions for study variables and clinical outcomes were predefined. After the DCFs were completed,

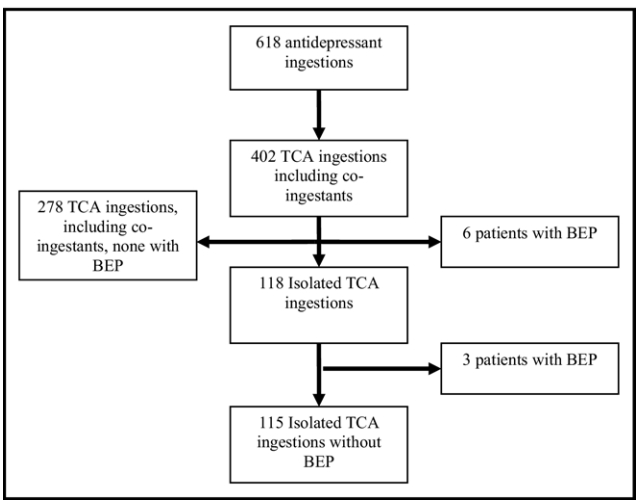

Figure 2. Flow diagram of patients involved in the study.

they were entered into a spreadsheet for analysis. The reviewers were blinded to the study objective.

The following outcomes were recorded for each subject: mortality, dysrhythmia (i.e., wide-complex tachycardia, ventricular tachycardia, ventricular fibrillation, Torsade de Pointes, atrial fibrillation, atrial flutter, or second- or third-degree block), widened QRS (>120 ms), hypotension (i.e., systolic blood pressure <90 mm Hg), seizure, endotracheal intubation, and intensive care unit admission. We also recorded the following TCA-induced clinical effects: tachycardia, central nervous system depression, and presence of a R wave >3 mm in lead aVR.