# Amitriptyline Toxicity Mimicking ST Segment Elevation Myocardial Infarction: A Case Report And Review Of The Literature

S H Jung, C Ugwu, N Hussain

**Citation**

S H Jung, C Ugwu, N Hussain. *Amitriptyline Toxicity Mimicking ST Segment Elevation Myocardial Infarction: A Case Report And Review Of The Literature* . The Internet Journal of Cardiology. 2013 Volume 11 Number 1.

**Abstract**

Brugada syndrome was for the first time described in 1992 by Brugada P et al. in patients with aborted recurrent episodes of sudden death. Since then association of Brugada syndrome with fatal arrhythmias and sudden cardiac death has been well established. Recently, drug induced Brugada wave pattern (BWP) has been reported in literature and its clinical significane remains unknown. In this article we have presented a case of amitriptyline toxicity related BWP mimicking myocardial infarction and have discussed complete resolution of EKG changes with sodium bicarbonate treatment.

## INTRODUCTION

Clinical and EKG characteristic of Brugada syndrome were described for the first time in 1992 by Brugada P et al. when they studied six male and two female patients with aborted recurrent episodes of sudden death. Later on these EKG characteristics and clinical presentations were recognized as “Brugada syndrome”. Brugada syndrome is characterized by coved or saddle ST segment elevation in at least two right precordial chest leads (V1-V3) with a right bundle branch block pattern in absence of any ischemia, structural heart disease or electrolyte imbalance. Association of Brugada syndrome with fatal arrhythmias and sudden cardiac death has been well established. Recently, drug induced Brugada wave pattern (BWP) or unmasking of underlying Brugada syndrome has been described in the literature. The clinical significance of drug induced BWP is not known. In this report, we describe a case of a young male with amitriptyline induced BWP who showed an excellent treatment response to sodium bicarbonate treatment.

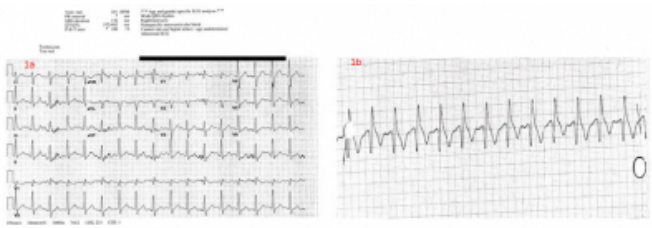
## CASE PRESENTATION

A 42 year old Hispanic male with a past medical history of bipolar disorder, polysubstance abuse, alcohol abuse and recently diagnosed co-infection of hepatitis C and HIV was brought to the emergency department after being found unconscious at home for four hours. The last time the patient was seen awake and alert was almost eight hours prior to presentation. At the time of presentation, patient was taking amitriptyline, buprenorphine with naloxone, fluoxetine, and buspirone. Patient had no family history of sudden cardiac death. Vital signs at the time of presentation were: heart rate of 117 beats per minute, blood pressure 119/65 mm Hg, temperature 99.2 Fahrenheit (37.33 C), and respiratory rate of 24 per minute. Patient was saturating 95% on room air, arterial blood gas analysis revealed PH of 7.31(7.35-7.45), pCO2 54.4 mm Hg (35.0-45.0), pO2 91.0 mm Hg (80-105), HCO3 27.0 meq/liter (22-28). Upon physical examination, patient was unresponsive with a GCS score of 3; pupils were reactive to light; lungs were clear to auscultation; heart rhythm was regular with no murmur, rub or gallop. Patient was immediately intubated for airway protection and central line was placed. Initial diagnostic workup including complete blood count, comprehensive metabolic panel, coagulation profile, cardiac troponins, chest X-ray, abdominal X-ray, serum ammonia was within normal limit. EKG demonstrated wide QRS rhythm and rightward axis deviation without any ST-T wave changes (Figure 1a). Urine toxicology screen was positive for cocaine, opiates and phencyclidine. After discussion with the poison control and after finding an empty bottle of amitriptyline at home clinical diagnosis of possible amitriptyline toxicity was made and no gastric lavage was attempted considering at least more than four to eight hours since ingestion had passed. Serum ethanol, isopropyl alcohol, ethylene glycol, valproic acid, phenobarbital, carbamazepine, lithium, acetaminophen, and salicylate levels were found to be with

in normal limits. Assay for serum tricyclic antidepressant revealed a level greater than 1000 ng/ml. Serum osmolality was 296 mili-osmole/kg (280-300). While initial diagnostic workup was being done, patient had three episodes of generalized tonic-clonic seizures, each episode lasting for a few seconds. A CT scan of head was performed which ruled out any acute intracranial abnormality. Following seizure episodes, patient became hypotensive with a blood pressure of 57/34 mm Hg. Three liters of intravenous normal saline bolus mixed with sodium bicarbonate was given followed by continuous infusion. Norepinephrine, epinephrine and dobutamine were started to support blood pressure. After the first seizure, tele-monitor was noted to demonstrate QT prolongation and possible ST segment elevation as shown in figure 1b. Serial EKGs showed increased QT interval, broadened QRS of 106 (figure 1c) and 150 mili-seconds (1d), and significant coved ST segment elevation in V1 to V3 with a negative T wave (Brugada wave) (Figure1c&1d). Code 42 was called for possible acute coronary syndrome but considering patient was on three pressors and was having recurrent seizures in a setting of TCA over dosage, patient was deemed not to be a candidate for any acute coronary intervention. Initial and serial troponin levels were within normal limits. Patient was treated with continued sodium bicarbonate infusion; a total of 700 meq of sodium bicarbonate was given. Subsequently transthoracic echocardiogram was done that revealed normal left ventricular systolic function and ejection fraction. Subsequently, patient regained consciousness on day 2 and was successfully extubated on day 4. Patient was transferred to the psychiatry floors for further care where he did well and was discharged to follow up on outpatient basis. Subsequently patient underwent non-invasive cardiac stress test which was found to be within normal limit.

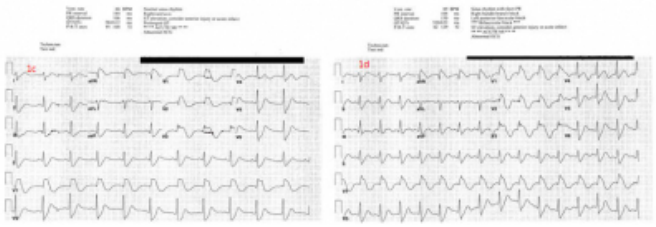
### Figure 1ab

1a- EKG at the time of presentation shows wide QRS complexes, rightward axis deviation, 1b- shows the tele monitor strip demonstrating the wide QRS complexes and possible ST segment elevation



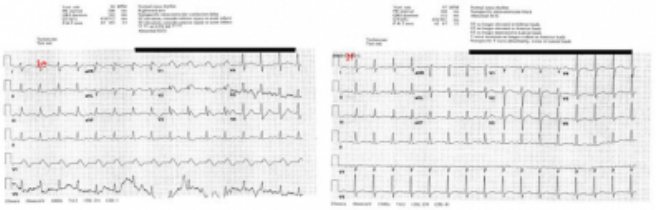
### Figure 1cd

1c- EKG 3 hours after admission shows rightward axis, prolonged QT, right bundle branch block pattern and coved ST segment elevation of 7mm with T wave inversion in lead V1, V2, V3, 1d- EKG 3.15 hours after the admission shows right bundle branch block, left posterior fascicular block and ST segment elevation of more than 7mm, the Brugada pattern can be seen



### Figure 1ef

1e- EKG 3.30 hours after admission shows rightward axis, nonspecific intraventricular conduction delay and ST segment elevation in anterior chest leads and in lead III& aVF, 1f- EKG 12 hours after admission shows resolution of the ST segment elevation



## DISCUSSION

Brugada syndrome (observed in lead V1 through V3) is believed to be a result of genetic myocardial sodium dysfunction (2); mutation of SCNA5 gene leading to an abnormality in alpha subunit of the sodium channel (3) is thought to be the most common pathogenic defect underlying Brugada syndrome. Brugada syndrome is transmitted in autosomal dominant manner with an incomplete penetrance and effects male population more commonly (4) and has an incidence rate ranging from 5-66 per 10,000 (1, 5). Three configurations for Brugada syndrome have been described in literature (6). Type I is characterized by coved ST segment elevation of at least 2mm above the base line with a negative T wave (6), type II also has at least greater than 2mm ST segment elevation but with gradual descent (ST stays 1mm above baseline) and is followed by a positive or biphasic T wave resulting in a saddleback configuration (6). Type III has a coved or saddleback appearance with a ST segment elevation of less than 1 mm (6). Type II and III require conversion to type 1

with sodium channel blocking agent to be diagnostic of Brugada syndrome (7). Patients with Brugada syndrome are at increased risk of cardiac arrhythmias and sudden cardiac death (7, 8). The clinical significance of Brugada wave pattern observed in setting of drugs toxicities has not been established.

Various drugs from antidepressant family including tricyclic (TCA), tetracyclic and serotonin reuptake inhibitors and many other agents including cocaine, lithium, antihistaminic and antipsychotic toxicity related Brugada wave pattern have been described (9-20). The incidence of TCA induced Brugada wave pattern has been reported to be less than 3% in cases of TCA toxicity (21).

In our patient, in addition to TCA toxicity, the urine toxicology screen was also positive for cocaine and PCP. Both TCA intoxication and use of cocaine could have been the cause of type1 BWP seen in our patient. Since the clinical features of toxicity in our patient were consistent with TCA over dosage, the chances that PCP had any contribution to BWP observed in our patient are probably minimal and further PCP related BWP has never been described which also makes our suspicion less likely. One of the serial EKGs (figure 1e) in our patient demonstrated an ST elevation in lead III and aVF and it may have been a result of nonspecific ST-T wave changes observed in a setting of TCA toxicity. Both BWP and ST elevation in leads III and aVF disappeared after continued sodium bicarbonate infusion (700 meq) which confirms that TCA was most likely the cause of EKG changes observed in our patient.

TCA induced reduction in the inward sodium current and a prominent outward current is believed to cause transmural heterogeneity in the action potential duration which accounts for the ST segment elevation observed in leads V1–V3 in setting of TCA toxicity (22, 23). Cocaine is believed to cause BWP through same sodium channel blocking properties (24).

Drug toxicities can not only cause the BWP, but may also uncover the underlying true Brugada syndrome. Whether patients with drug toxicity related BWP need electrophysiologic evaluation and insertion of cardioverter defibrillators for inducible ventricular arrhythmias is still unclear (25). Conflicting literature is available on clinical significance of drug toxicity related BWP (25, 26), most consider it to be benign whereas others believe that electrophysiologic evaluation may be necessary if there is a family history of sudden cardiac death (6). According to some authors, if patients with drug-induced BWP present with signs or symptoms related to Brugada syndrome such as syncope, arrhythmias, they should receive ICD (7). Electrophysiologic evaluation in our patient was not done as patient had no family history of sudden cardiac death and BWP was considered to be a benign process.

Sodium bicarbonate treatment in TCA toxicity serves two folds; first, it increases the protein binding of circulating TCA thereby decreasing the tissue TCA levels and second it increases the sodium gradient between extracellular and the cellular spaces (27). Our patient showed a dramatic response to sodium bicarbonate treatment.

In conclusion, recognition of drug induced BWP in appropriate clinical context will prevent major morbidities related to unnecessary urgent cardiac catheterization in such patients. Future trials are needed to address, whether patients with drugs induced BWP should undergo routine electrophysiologic evaluation for inducible ventricular arrhythmias and to determine the prognostic significance of drug-induced BWP.

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## Author Information

**Su Hyeon Jung, MD**
Saint Joseph Hospital, Department of Internal Medicine
Chicago, Illinois, USA

**Chukwuma Ugwu, MD**
Saint Joseph Hospital, Department of Internal Medicine
Chicago, Illinois, USA

**Nasir Hussain, MD**
Saint Joseph Hospital, Department of Internal Medicine
Chicago, Illinois, USA
NHussain@reshealthcare.org