Brugada electrocardiographic pattern in carbon monoxide poisoning

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Carbon monoxide (CO) poisoning is the most common type of accidental poisoning in the United States, contributing to an estimated 15,000 emergency department visits and 500 deaths in the United States each year [1]. The signs and symptoms of CO poisoning are diverse, ranging from headache, lethargy, dizziness, nausea and confusion to cardiac and neurological disturbances. Cardiovascular complications of CO poisoning include myocardial ischemia, left ventricular dysfunction, or arrhythmias. We report the first case of Brugada electrocardiographic pattern (BEP) in CO poisoning in the English literature.

A 56-year-old hispanic male was found unconscious in his home by his son who called the emergency medical services. Patient regained consciousness while receiving 100% oxygen by means of non rebreather reservoir face mask in the ambulance. Upon arrival to the emergency room, the patient was awake, but complained of mild headache and dizziness. He denied any chest pain, palpitation or shortness of breath. Past medical history was significant for dyslipidemia, being treated with simvastatin. Family history was negative for sudden cardiac death. Vital signs on admission showed a temperature of 100.4 F, heart rate of 110 beats/minute, blood pressure of 129/89 mm Hg, respiratory rate of 24 per minute, with oxygen saturation of 100% on non-rebreather mask delivering 100% oxygen. Arterial blood gas analysis by co-oximetry showed pH 7.48, pCO_2 33 mm Hg, pO_2 250 mm Hg, HCO_3 24.6 mmol/l, and oxygen saturation of 99%. Carboxyhemoglobin (COHb) level on admission was 25.2%. Creatine kinase, creatine kinase-MB isoenzyme, and troponin I was within normal limits. Electrocardiogram (ECG) done in emergency room showed sinus tachycardia at 104 beats per minute, left axis deviation, and ST-segment elevation of 3.5 mm in V1-V2 with a saddleback appearance, characteristic of type 2 BEP (Figure 1 A). Urine toxicology screen was negative for cocaine, amphetamines, opiates and benzodiazepines. Serum anion gap was normal and no osmolal gap was noted. Portable chest radiograph was within normal limits. Transthoracic 2-dimensional echocardiogram (ECHO) showed normal left ventricular systolic function, and no regional wall motion abnormalities. The patient was admitted to telemetry unit and administered 3 cycles of hyperbaric-oxygen therapy (HBOT) within a 24-hour period. Repeat ECG after HBOT showed resolution of the bru-

gada pattern (Figure 1 B). The patient subsequently underwent an exercise nuclear stress test that was negative for ischemia.

Cardiac toxicity of CO is caused by acute, generalized tissue hypoxia and toxic effects on myocardial mitochondria [2]. The affinity of hemoglobin for CO is 200 to 250 times greater than its affinity for oxygen. This results in competitive inhibition of oxygen release resulting in reduced oxygen delivery to tissues, and subsequent tissue hypoxia [3]. *In vitro*, CO binds to cytochrome oxidase of the electron transport chain resulting in asphyxiation at the cellular level [4]. High concentrations of CO result in oxidative stress, which could reduce nitric oxide levels, causing direct myocardial injury [3, 5].

Myocardial injury occurs frequently in patients with CO poisoning and is a significant predictor of both short term and long term mortality [6, 7]. Early deaths after CO exposure may be due to cardiac arrhythmias as CO exposure lowers the threshold for malignant ventricular arrhythmias [8-10]. CO causes negative inotropic effect which results in increased left ventricular end-diastolic pressure and decreased stroke index [11]. ECG abnormalities that have been described in cases of carbon monoxide poisoning include ST-segment and T-wave abnormalities, premature atrial and ventricular contractions, and atrial and ventricular fibrillation [12]. Increased QT dispersion, P-wave dispersion and corrected QT interval and reversible right bundle branch block have also been demonstrated in patients with CO poisoning [13-16]. ST segment elevation is a rare presentation, and most of these cases with myocardial infarction have revealed non-occlusive or normal coronary arteries [2], although total occlusion of the left anterior descending artery has also been reported [17].

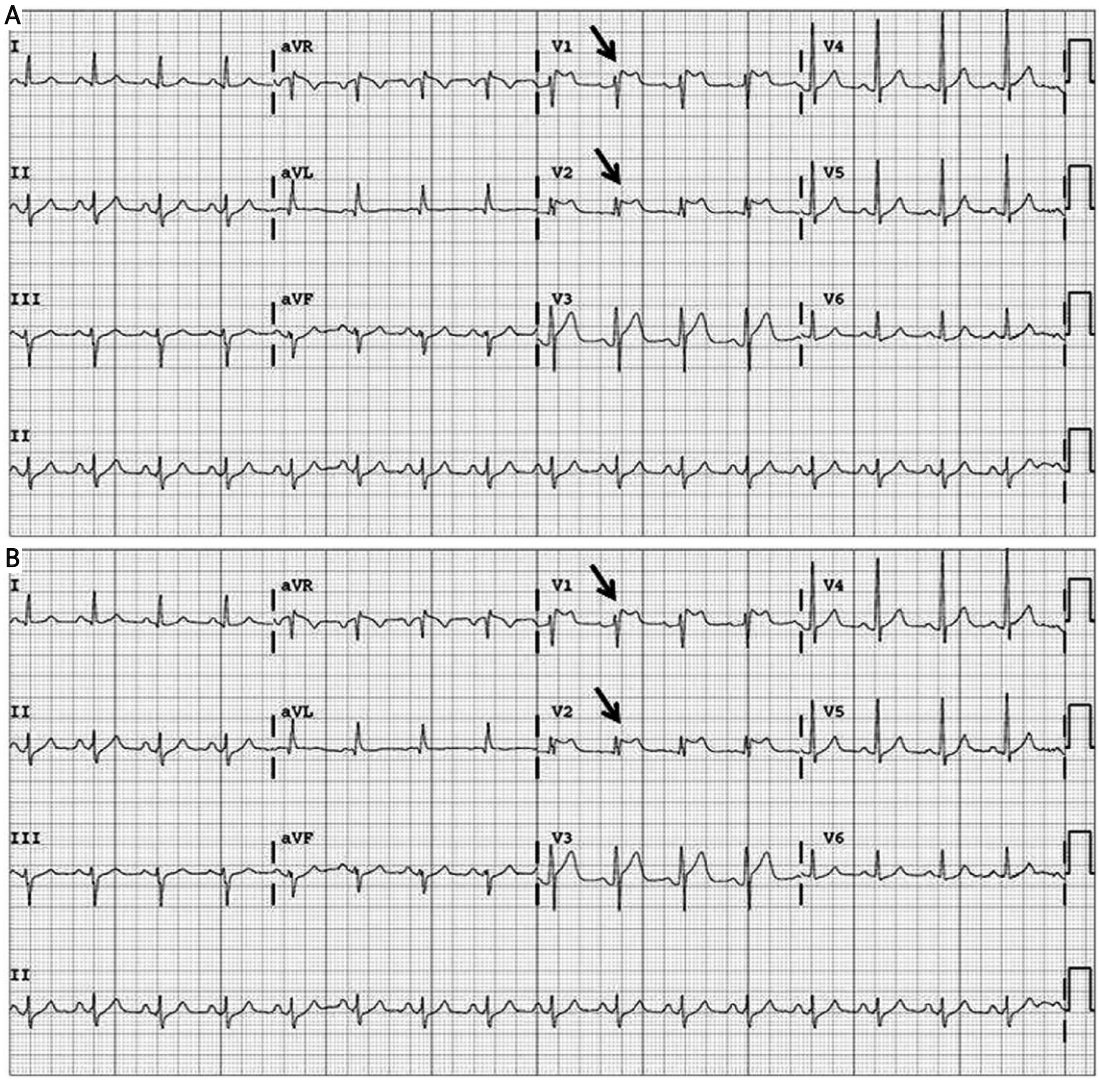

Figure 1. A – Initial ECG on admission that shows the following: sinus tachycardia, left axis deviation, and ST-segment elevation of 3.5 mm in V1-V2 with a saddleback appearance, characteristic of type 2 Brugada pattern. **B** – Repeat ECG after hyperbaric therapy showing resolution of the Brugada pattern

In a study of 83 young healthy patients with CO poisoning, mean age 27 years, and with mean carboxyhemoglobin level of 34.4 %, electrocardiographic changes included sinus tachycardia in 26.5% of patients, and diagnostic ischemic ECG changes in 14.4% of patients [18]. In a study of 230 patients, mean age 47 years, and 72% men, with moderate to severe CO poisoning who were treated with HBOT, myocardial injury defined by elevated biomarkers and/or diagnostic electrocardiographic changes was reported in 85 (37%) patients [19]. Of the 230 patients, 7% had a previous history of myocardial infarction, and 3% had previous revascularization. Ischemic electrocardiographic changes were seen in 30%, and positive biomarkers in 35% of patients, while only 16% had a normal electrocardiogram. In-hospital mortality was 5%. Predictors of myocardial injury included male gender, a GCS score of ≤ 14, and hypertension. Two patterns of myocardial injury were indentified: younger patients with few cardiac risk factors but severe CO poisoning with global left ventricular dysfunction consistent with stunned myocardium as a result of CO poisoning; and a second group of older patients with a higher frequency of cardiac risk factors with regional wall motion abnormalities resulting from unmasking of underlying CAD by creating supply/demand mismatch. At a median follow-up of 7.6 years, there were 54 deaths (24%) [7]. Of the 85 patients with myocardial injury from CO poisoning, 32 (38%) eventually died compared with 22 (15%) of 145 patients without myocardial injury (p = 0.009).

Brugada pattern has not been reported with CO poisoning in the English literature. The Brugada syndrome is a clinical and electrocardiographic entity consisting of right bundle-branch block and unusual ST-segment elevation in the right precordial leads (V1 to V3) and responsible for at least 4-12% of all sudden deaths and at least 20% of sudden deaths in patients with structurally normal hearts [20]. Mutations in SCN5A, a cardiac sodium channel gene, transmitted in an autosomal dominant pattern are implicated as a cause [21]. Three different electrocardiographic patterns related to this entity have been described (Figure 2): a) type I, characterized by a coved-type ST-segment elevation ≥ 2 mm in more than one right precordial lead (V1-V3), followed by negative T wave; b) type II, characterized by ST-segment elevation ≥ 2 mm in right precordial leads followed by positive or biphasic T waves, resulting in a saddleback configuration; and c) type III, defined as any of the 2 previous types if ST-segment elevation is ≤ 1 mm. Brugada syndrome should only be established when the type I ECG pattern is documented in combination with at least one of the following clinical criteria: documented ventricular fibrillation (VF), documented polymorphic ventricular tachycardia (VT), inducible ventricular arrhythmias during electrophysiological study, syncope or nocturnal agonal respiration, a family history of sudden cardiac death at < 45 years of age, or type I ECG pattern in other family members [20]. However, BEP in absence of clinical symptoms can be produced by sodium channel blockers, a febrile state, vagotonic agents, alpha adrenergic agonists, β adrenergic blockers, tricyclic or tetracyclic antidepressants, a combination of glucose and insulin, hyperkalemia, hypokalemia, hypercalcemia and alcohol and cocaine toxicity [22, 23]. Recent data demonstrate that a type I BEP pattern alone, even when other clinical criteria are not fulfilled, can be associated with sudden cardiac death during follow up [24].

The exact mechanism of interaction of CO with the sodium channels is unknown and needs further study. Given the effect of myocardial injury on outcome of CO poisoning, patients with BEP pattern in the setting of CO poisoning should be considered at risk for ventricular arrhythmias and sudden death. Treatment of CO poisoning begins with inhalation of supplemental oxygen with non-re-

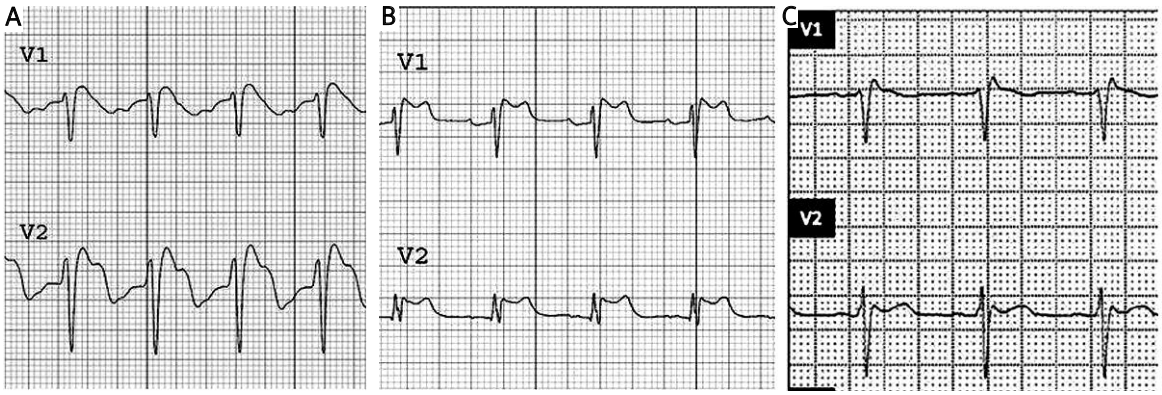

Figure 2. Three different Brugada electrocardiographic patterns as shown in this figure: type 1 – coved-type ST-segment elevation ≥ 2 mm in more than one right precordial lead followed by negative T wave; type 2 – ST-segment elevation ≥ 2 mm in right precordial leads followed by positive or biphasic T waves, resulting in a saddleback configuration; type 3 – any of the 2 previous types if ST-segment elevation is ≤ 1 mm

breather mask and aggressive supportive care. The most effective way to treat CO poisoning is HBOT. HBOT has been proven to reduce neurological after CO poisoning, but data on efficacy of HBOT for prevention of myocardial injury is limited [25]. In a case series of 18 consecutive patients with cardiac arrest complicating CO poisoning, it was uniformly fatal, despite administration of HBOT after initial resuscitation [26]. Whether HBOT may limit myocardial injury or infarct size in patients without initial cardiac arrest is unknown.

Current indications for HBOT in CO poisoning remain controversial, although most would agree that HBOT is indicated in patients who are comatose or neurologically abnormal, loss of consciousness with their exposure, or have cardiac dysfunction. The current indications for HBOT in CO poisoning from cardiovascular standpoint are cardiac ischemia, arrhythmias, or carboxyhemoglobin level > 20% with underlying coronary artery disease. Pregnancy with an elevated COHb level > 15% to 20% is also considered an indication for HBOT. Patients who have persistent symptoms despite normobaric oxygen therapy, metabolic acidosis, abnormalities on neuropsychometric testing, significantly elevated levels or with longer exposure should be considered for HBOT [10]. Even in the absence of arrhythmias or myocardial ischemia, BEP in a patient with CO poisoning may be considered for HBOT.

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