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Case report

BRUGADA PATTERN IN HEROIN ADDICTION: SYNDROME OR PHENOCOPY?

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ABSTRACT

Brugada phenocopies (BrPs) are clinical entities that show an electrocardiogram (ECG) pattern similar to what is observed in Brugada syndrome (BrS). They are caused by different clinical conditions. We describe a case of BrP in a man that developed acute kidney failure secondary to rhabdomyolysis, after heroin addiction. His initial ECG showed Brugada type 1 pattern resolved after hemodialytic treatment. A provocative test with ajmaline, which resulted negative, was performed to confirm the diagnosis. BrPs can mimic a true BrS and a fast recognition of these clinical and electrocardiographic findings may avoid diagnostic mistakes thus preventing unnecessary or inaccurate treatments

1. Introduction

BrPs are a group of heterogeneous conditions that are not simple to distinguish from true congenital BrS. They show identical ECG patterns but are elicited by various underlying clinical conditions such as electrolyte disturbances, drugs or myocardial ischemia. In this case-report, we describe the case of BrP occurring in a man with heroin addiction who developed hyperkalemia for acute renal failure due to rhabdomyolysis.

2. Material and methods

A 41-year-old Caucasian man went to the emergency department of a hospital near Palermo for general discomfort following use of heroin.
The patient talked about a lumbosacral trauma that occurred two days before the hospitalization and heroin consumption for analgesic purpose.
The family history was negative for cardiovascular and congenital heart diseases or sudden cardiac death. He has a long history of drug addiction along with alcohol, cannabis and heroin abuse.
When he was admitted, he was very excitable and showed profuse sweating, miotic pupils, shallow and frequent breathing. He complained of widespread muscle pain.
The patient was anuric, no fever was found (Temp. 36 ° C) and his blood pressure was 180/138 mmHg with a heart rate of 61 bpm.
His initial lab tests showed urea 102 mg/dl, serum creatinine 6.56 mg/dl and potassium 8.5 mmol/L along with a severe metabolic acidosis (pH = 7.27, pO2= 83 mmHg, pCO2= 29 mmHg, HCO3 = 13.6 mmol/L, Base deficit=-13.9 mmol/L, Lactate 4.3 mmol/L). The increased levels of creatine phosphokinase (CPK> 2000 U / L) and transaminase (AST/ALT 5684/4305 U/L) and the presence of myoglobinuria revealed a rhabdomyolysis that was responsible for AKI (Acute Kidney Injury).
The first ECG showed sinus rhythm, left axis deviation, elevation of the ST "Coved-Type" segment in V1-V3 (Figure 1). The troponin I at the admission was 356 ng / ml (normal values <14 ng / ml). The ECG interpretation and high troponin I levels created a differential diagnosis between an acute antero-septal ST-segment elevation myocardial infarction and a Brugada ECG pattern. The lack of “mirror” ST-segment alterations in the inferior leads and the lack of wall movement abnormalities at ultrasound heart scan along with the stability of troponin I values, allowed us to exclude an acute coronary syndrome.
The patient was treated by administration of calcium gluconate IV, dextrose IV with rapid insulin and sodium bicarbonate. Additionally, naloxone IV was administered to reduce the symptoms of heroin intoxication.

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Due to the persistence of serious clinical conditions, the patient was admitted to our Nephrology ward, where he promptly underwent hemodialysis treatment that was repeated in the following days. We therefore observed a gradual improvement in serum rhabdomyolysis markers and a recovery of diuresis and a full normalization of the ST segment alterations with the disappearance of the typical Brugada ECG-graphic pattern (Figure 2).

Toxicological screening in serum and urine was positive for opioids and cannabinoids. For the appearance of withdrawal syndrome symptoms, methadone hydrochloride was also used.

To differentiate a BrS from a BrP, provocative pharmacological tests were performed with ajmaline e.v. at the dose of 1 mg/kg, with negative results, confirming the diagnosis of BrP. (Figure 3) ECG-graphic monitoring during hospitalization did not detect the presence of arrhythmias and the patient was discharged in improved general clinical conditions, with valid diuresis and resolution of rhabdomyolysis.

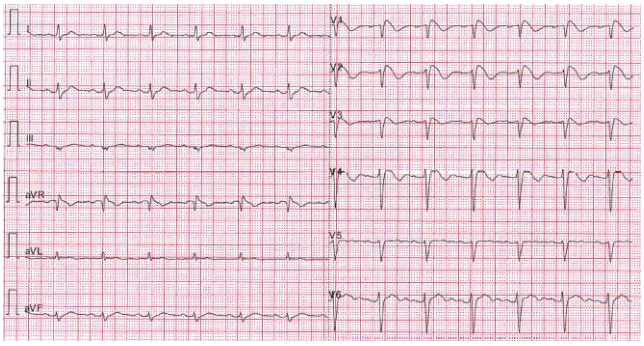

Figure 1. Electrocardiogram performed in the emergency room at admission. It shows sinus bradycardia, left axis deviation, elevation of the ST "Coved-Type" segment in V1-V3.

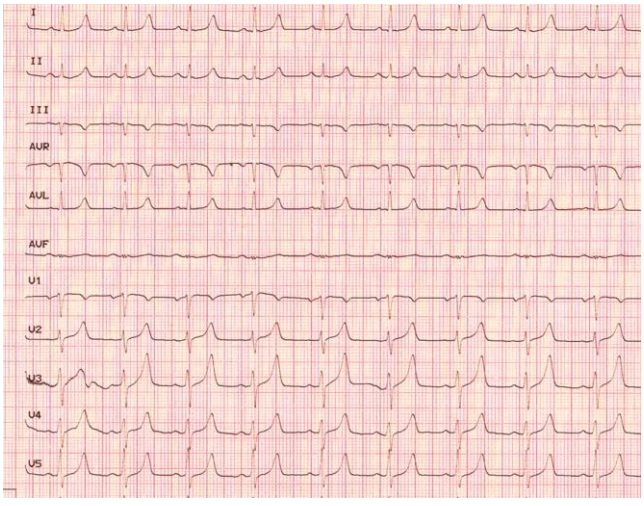

Figure 2. Electrocardiogram performed after hemodialysis. The elevation of the ST in V1 and V2 completely disappeared.

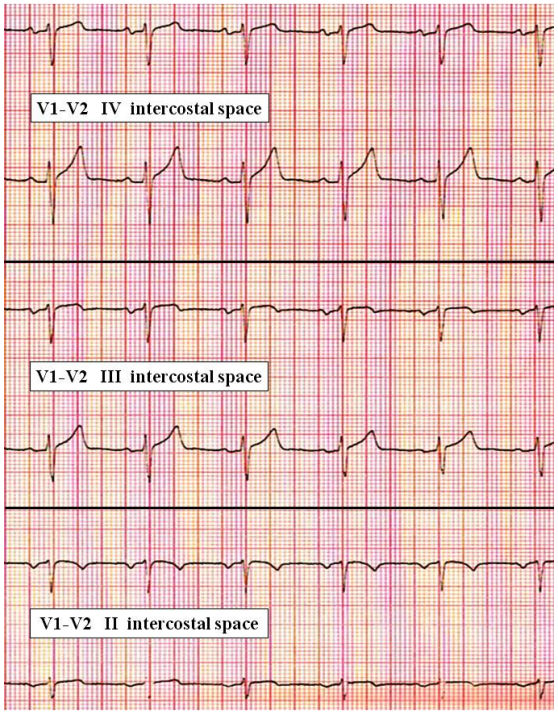

Figure 3. Electrocardiogram performed after hemodialysis. The elevation of the ST in V1 and V2 completely disappeared.

3. Discussion

This case reports a paradigmatic example of a Brugada phenocopy in a heroin addicted subject with Acute Kidney Injury due to rhabdomyolysis. Several mechanisms are able to induce rhabdomyolysis in heroin addicts: myotoxic effect of quinine, an adulterant substance found in heroin; direct cyto-toxic effect of narcotics by alteration of membrane transporters; prolonged immobility or a state of coma following the inoculation of "dose". The lack of liquids and food supply during these situations causes a reduction in the production of adenosine triphosphate (ATP), dehydration and consequent increased risk of rhabdomyolysis (1).

Severe renal failure represents the main complication of rhabdomyolysis, that may develop in about 50% of cases, increasing the mortality rate (2).

Brugada phenocopies are clinical entities, first defined by Baranchuck and colleagues, that present an identical ECG pattern of Brugada Syndrome but are elicited by various clinical circumstances (3). A lack of family and personal history for syncope or sudden death, the disappearance of ECG Brugada pattern after resolution of underlying conditions and a negative provocative challenge with a sodium channel blocker can be the main diagnostic criteria to define a Brugada phenocopy in order to differentiate this clinical condition from Brugada syndrome. The negative genetic test for SCN5A mutation is not a mandatory criterion because it is identified in only 20-30% of the people that are proved to be affected by Brugada syndrome (4).

In our clinical case, Brugada phenocopy may be due to ECG-graphic alterations induced by the heroin overload. Heroin intoxication could be related to a greater risk of sudden cardiac death.

Furthermore, heroin-induced ECG alterations have been reported in over 55% of heroin addicts, which are mainly represented by QTc prolongation and bradyarrhythmia (5).

There are several factors that could have played an important role in the development of this Brugada ECG-graphic pattern. Hyperkaliemia, along with rhabdomyolysis, acute renal failure and acidosis, has been identified as a metabolic condition that can mimic the Brugada ECG pattern by decreasing the resting membrane potential of myocardial cells, which causes an inactivation of the voltage-dependent sodium channels responsible for myocardial depolarization. Thus, we can observe an alteration between the flux of sodium ions entering and the flow of potassium ions leaving the myocardiocyte, with the outflow predominance of the potassium ion flux (Ito current) (6)(7).

The negative effects of high potassium levels seem to be more marked in the myocardial cells of the right ventricular outflow tract (RVOT), involving more of the epicardium cells than the endocardium ones, as they are more sensitive to the harmful effects induced by the hyperkalemia. This determines a delayed depolarization causing an elevation of the ST segment in the right precordial derivations, simulating the alterations of the sodium channels typical of Brugada syndrome. Data available in literature have shown that typical Brugada ECG patterns occur when potassium levels are between 6.0 and 8.8 mmol / L (8).

Our patient did not report any heart disease or genetic background of sudden cardiac death or cardiovascular disease and the type 1 Brugada ECG pattern disappeared after the hemodialysis treatment that led to the resolution of rhabdomyolysis. These characteristics are appealing for a BrP rather than a BrS, confirming the negativity of the drug test with ajmaline (Figure 3). A morphological classification system divides BrPs into a type 1 and type 2 BrP according to the ECG pattern. These two categories include A, B and C qualifiers. Our case could be included in the International Registry of Brugada Phenocopies as a type-1, Class A (9). (Table 1)

Type		Class	
Type 1 BrP	Brugada Phenocopy with typical type 1 Brugada ECG pattern	Class A	All mandatory BrP diagnostic criteria are satisfied including provocative challenge with sodium channel blocker such as ajmaline, flecainide, or procainamide
Type 2 BrP	Brugada Phenocopy with typical type 2 Brugada ECG pattern	Class B	Highly suspected BrP; however, not all mandatory criteria are complete
		Class C	Highly suspected BrP; however, mandatory provocative challenge with sodium channel blocker not justified

Table 1. Brugada Phenocopy classification System.

An international registry and online educational portal provide an updated registry of BrP cases along with the diagnostic criteria (www.brugadaphenocopy.com).

In conclusion, this case allows us to underline the differential diagnosis between Brugada syndrome and Brugada phenocopy due to metabolic alterations, which can also simulate a myocardial infarction with ST segment elevation. Hence, a systematic approach is crucial to avoid diagnostic errors and to obtain a rapid recognition of this clinical and electrocardiographic entity.

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