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Case Report

Use of therapeutic hypothermia and extracorporeal life support after an unusual response to the ajmaline challenge in a patient with Brugada syndrome

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ABSTRACT

Background: Brugada syndrome is a cardiac disorder associated with a high risk of sudden cardiac death, especially in young subjects. The incidence and prevalence are likely underestimated. The diagnosis is based on a characteristic electrocardiography (ECG) pattern. The most commonly performed confirmatory test in cases of equivocal ECG is the intravenous ajmaline challenge. Although relatively safe, it carries the risk of ventricular arrhythmias that could potentially degenerate into a refractory electrical storm.

Case report: A 27-year-old man developed sustained ventricular fibrillation after ajmaline challenge. He was rescued on extracorporeal life support after 108 min of cardiopulmonary resuscitation. Extracorporeal life support allowed recovery of spontaneous circulation and resulted in a positive neurological outcome.

<Learning objective: This case is an example of how extracorporeal life support was instituted after prolonged and unsuccessful cardiopulmonary resuscitation resulting in a positive central neurological outcome.>

Introduction

Brugada syndrome (BS) is a cardiac disorder, with electrocardiographic features of pseudo-right bundle-branch block and persistent ST-segment elevation in leads V1–V3 with high risk of sudden cardiac death [1,2]. This disorder is genetically transmitted and mostly due to mutations in the gene encoding for the alpha-subunit of the cardiac sodium channel, SCN5A.

Intravenous ajmaline challenge (Class IA antiarrhythmic), using a protocol with fractionated drug administration is a widely accepted safe method to confirm the diagnosis of BS when the resting electrocardiogram (ECG) is not diagnostic. Despite the risk of induced ventricular dysrhythmias, ajmaline is considered the drug of choice given its short duration and higher sensitivity compared to other Na^+ channel blockers [3]. Ajmaline-induced ventricular arrhythmias are often refractory to electrical therapy thus requiring prolonged circulatory support.

We report a case of a sustained ventricular fibrillation (VF) after ajmaline challenge test in whom innovative strategies for treating cardiac arrest were used.

Case report

A 27-year-old asymptomatic male presented to our tertiary care center for BS testing due to his positive family history (brother diagnosed with BS). His past medical history included whooping cough at 3 months and a spontaneous pneumothorax at 17 years. An initial flecainide test (2 mg/kg for 10 min) was not fully diagnostic, but suggestive of BS due to ST elevation in V2 of 2 mm (Fig. 1). An ajmaline test was then performed.

A first ajmaline bolus of 0.7 mg/kg over 5 min was given intravenously but failed to unmask an ECG BS pattern. A second bolus of 1 mg/kg over 5 min was then administered. During the infusion, the patient suddenly developed a polymorphic ventricular tachycardia that rapidly degenerated into VF (Fig. 2). External defibrillation

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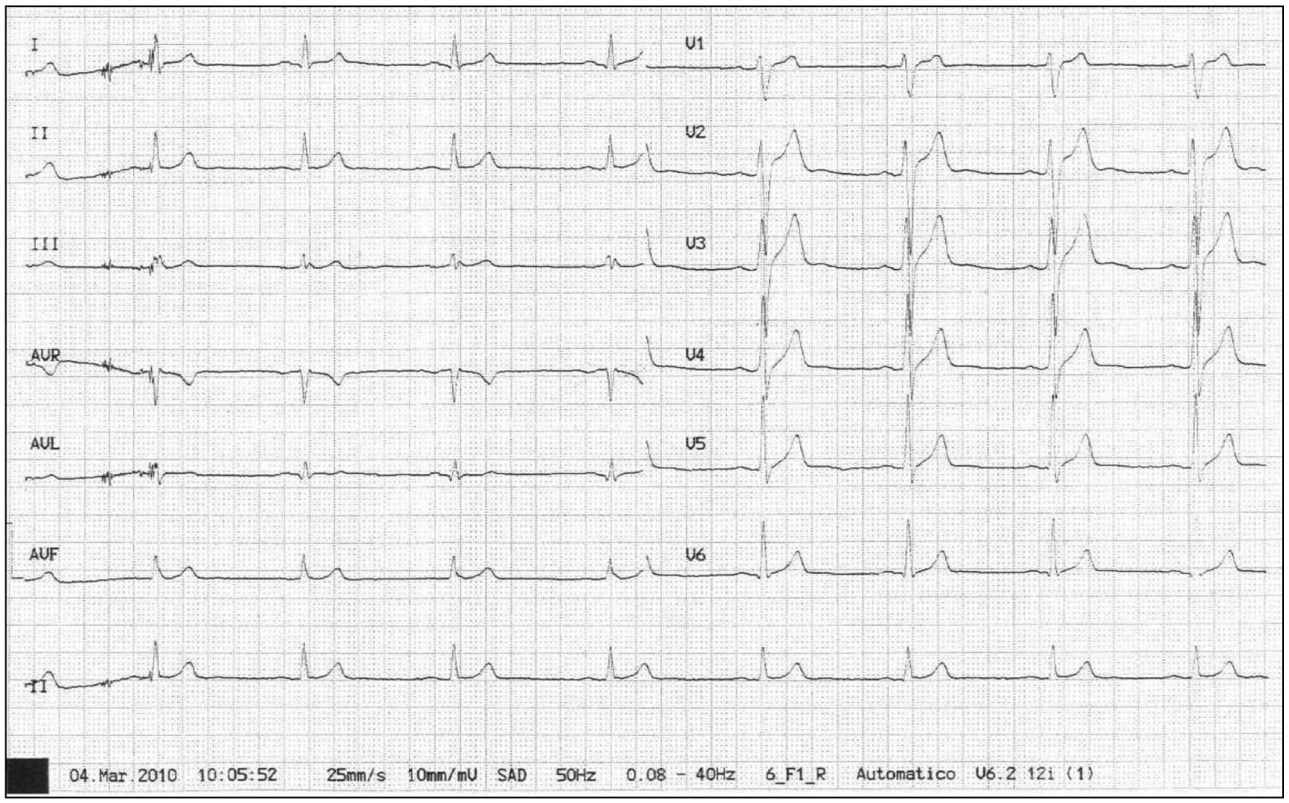
a)



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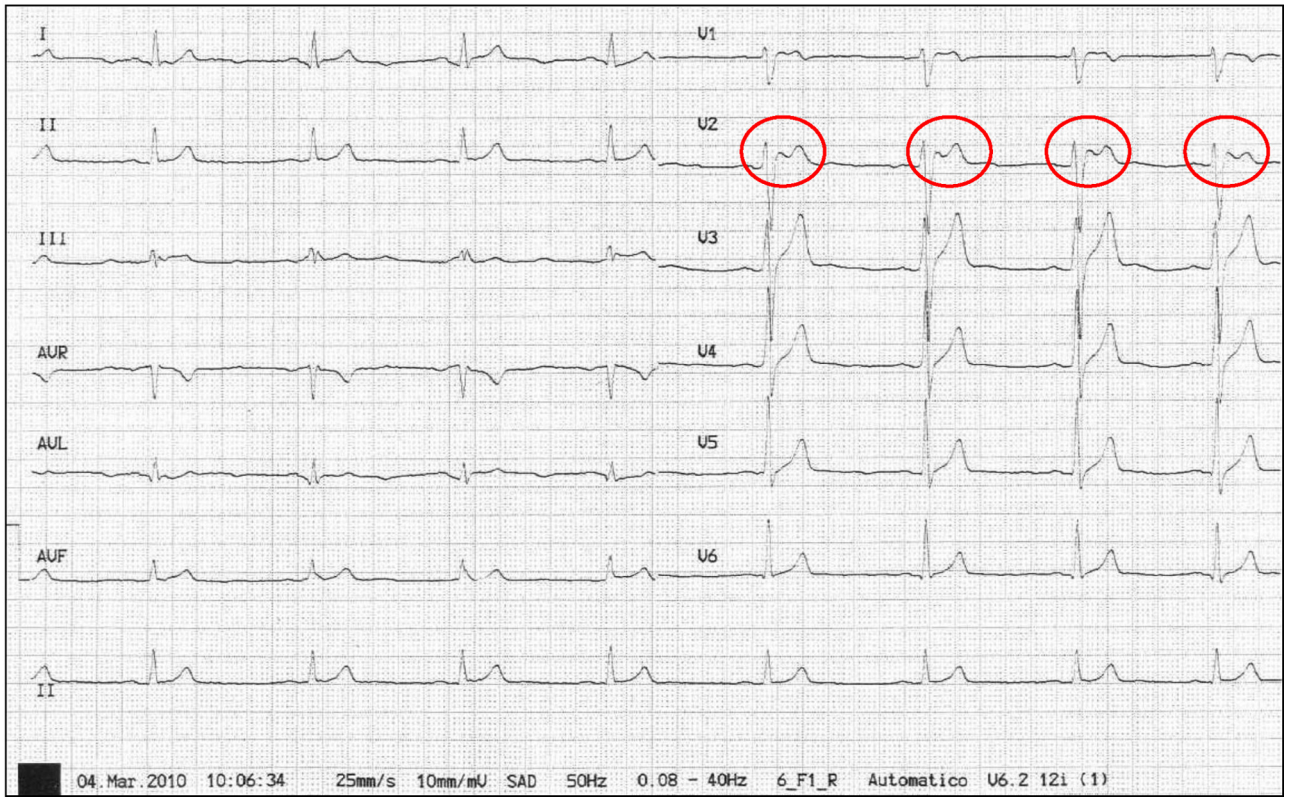

Fig. 1. Flecainide test (2 mg/kg for 10 min). Electrocardiogram: (a) baseline: sinus rhythm at 60 bpm. (b) At the end: sinus rhythm, ST elevation in V2 of 2 mm (very suggestive of Brugada syndrome).

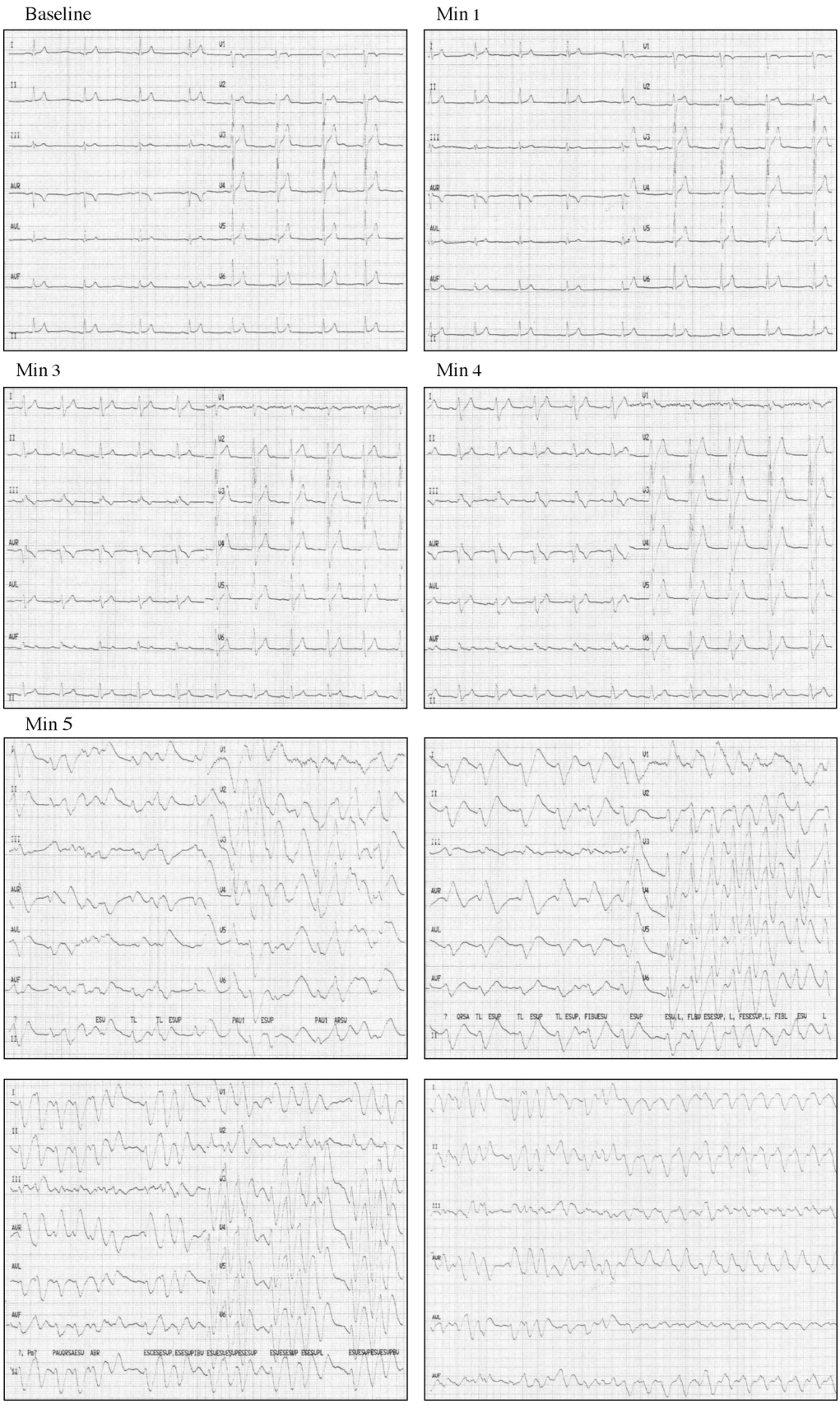

Fig. 2. Ajmaline test. In the first 4 min (a) electrocardiographic changes were recorded. (b) At the 5th minute the patient suddenly developed a polymorphic ventricular tachycardia that rapidly degenerated into ventricular fibrillation.

was unsuccessful and cardiopulmonary resuscitation (CPR) was started according to the European Resuscitation Council guidelines. During CPR, adrenaline was given at a rate of 1 mg every 4 min, followed by a continuous intravenous infusion of isoproterenol (10 μg/min). Hypertonic sodium bicarbonate was given at 2 meq./kg as a rapid intravenous bolus followed by an infusion of 250 meq./h of 8.4% sodium bicarbonate. Electrolyte replacement included: 1 g of calcium gluconate and 1.5 g of magnesium sulphate. The airway was secured with endotracheal intubation 6 min after CPR was started. A refractory electrical storm persisted after 20 min of CPR and 10 shocks; a 20% lipid emulsion infusion was started at this point at a rate of 0.25 mL kg^{-1} min^{-1} after 1 mL/kg bolus over 1 min. Quinidine was considered but was not available on the floor at this moment and a cardiac surgeon was consulted to place the patient on mechanical circulatory support [4,5].

For more effective chest compressions and not to discontinue CPR during surgical cannulation, an external cardiac compressor (Lund University Cardiac Arrest System, LUCAS™, Lund, Sweden) was used. Extracorporeal life support (ECLS) was finally instituted after 107 min of CPR and 53 unsuccessful defibrillation attempts. An extracorporeal membrane oxygenator (ECMO) circuit was used providing a flow between 3 and 4.5 l/min at 2415–3275 rpm, sweep of 7–3.5 l/min, and a variable inspired fraction of oxygen. Mild therapeutic hypothermia (MTH) was initiated for cerebral protection with a target temperature of 33 °C for 24 h followed by active rewarming at 0.25 °C/h to normothermia using the ECLS device [6]. The patient finally recovered a stable sinus rhythm, 118 min after ECLS initiation and pulmonary artery catheter was placed for hemodynamic monitoring at this point. Normal ventricular function was shown by transthoracic echocardiography at 24 h post-arrest.

ECLS was successfully weaned 43 h post-arrest and the patient decannulated. The patient was finally extubated 4 days later. Neurological examination at the time post-extubation revealed altered T5 sensation level, paresthesia, and weakness in both lower limbs, slight cognitive dysfunction characterized by slow ideation and minor difficulty in calculation. A nuclear magnetic resonance showed an intramedullary alteration at the level of medullar conus, suggesting an acute–subacute ischemia (Fig. 3). An implantable cardioverter-defibrillator was placed and the patient was then discharged to a specific neuro-rehabilitation center 21 days after the arrest. At 1-year follow-up, the patient presented with improved cognitive function and unchanged paraplegia.

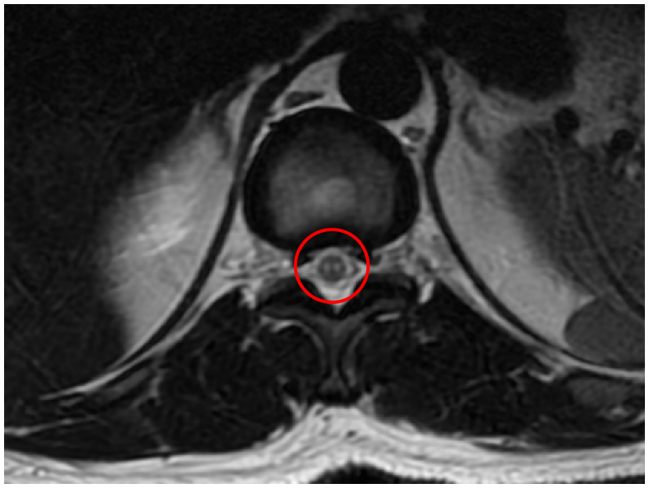

Fig. 3. Nuclear magnetic resonance imaging. Intramedullary alteration at the level of medullar conus, suggesting an acute–subacute ischemia.

Discussion

BS is genetically transmitted and mostly due to mutations in the gene encoding for the alpha-subunit of the cardiac sodium channel, SCN5A. Mutations in SCN5A gene lead to a decreased sodium current by encoding a dysfunctional alpha-subunit of the voltage-gated cardiac sodium channel, resulting in a modification of the ionic imbalance and a consequent change in the morphology of the action potential during phase 1. Class I antiarrhythmics are commonly used sodium channel blockers. Intravenous ajmaline challenge has been described as a safe test to unmask the ECG pattern of BS. Nevertheless, oral ajmaline poisoning may be lethal and 0.15% of patients undergoing intravenous ajmaline challenge develop sustained VF commonly terminated by a single external defibrillator shock [3]. Quinidine and isoproterenol have been reported to be a useful pharmacological treatment during refractory malignant ventricular dysrhythmias in BS, by rebalancing the ionic currents affected by this condition. Hypertonic sodium bicarbonate, electrolyte replacement, and a 20% lipid emulsion are key interventions in the early management of toxicity by these agents, but often not enough to prevent a refractory cardiac arrest (CA) unresponsive to conventional CPR.

In these circumstances, prolonged CPR may be necessary. Studies show that high-quality chest compressions are difficult to maintain for long periods, even when performed by trained hospital staff. Despite the setting, the environment, the response time, the equipment, and experienced hospital staff, resuscitation skills deteriorate over time. Mechanical devices are available in some countries and widely used by out-of-hospital cardiac arrest (OHCA) teams, but rarely used for in-hospital cardiac arrests (IHCAs). These help to maintain good quality chest compressions during prolonged periods, allow transportation, and interventional procedures such as percutaneous coronary intervention without interrupting compressions. However, a comparison of manual versus mechanical chest compressions did not show any outcome difference in OHCA [7].

IHCA has a reported initial survival rate of 38.6% with a survival at discharge of about 15.9% [8], with neurological prognostication, after recovery of spontaneous circulation, the main problem. The use of combined therapeutic techniques in IHCA and OHCA such as ECLS, MTH, and mitochondrial medicine with the addition of regionalization (specialized centers with expert care in CA) are helping to change the outcomes.

ECLS has been suggested as a therapeutic option in refractory CA since 1976. However, its use has remained limited to hypothermic CA and the perioperative period of cardiothoracic surgery due to the initial deceptive results. Recent miniaturized ECLS systems have permitted a wider use. Encouraging results have been published. In these studies, most cases were IHCA from toxic or cardiac causes, down time was close to zero, and survival with good neurological outcome up to 20–30% [9,10]. The aim of ECLS is to provide temporary perfusion to vital organs until injured myocardium recovers. Indications for ECLS rescue in a CA have not been clearly defined, but cardiotoxic drugs intoxication and severe accidental hypothermia are two widely accepted due to their reversibility. ECLS has been more often proposed as an ultimate rescue in prolonged CA and failing conventional CPR [11].

After recovery of spontaneous circulation, one of the main concerns is neurological outcome. In the past decade, mild hypothermia treatment has shown some degree of brain protection in patients post-CA, especially when due to shockable rhythms. Two positive large prospective randomized trials conducted in 2002 led

to the inclusion of MTH in the official guidelines as a therapeutic tool in the unconscious adult patients, with return to spontaneous circulation after OHCA due to shockable rhythms and, since 2010, it is also recommended after IHCA and CA due to non-shockable rhythms [12,13]. Some studies have shown that ECLS could provide both systemic cooling and hemodynamic support in cardiac arrest patients, but future research should evaluate its usefulness and safety [14].

In summary, MTH can be used safely in Brugada syndrome, reversing the Brugada phenotype by the prevention of fever and at the same time giving cerebral protection after cardiac arrest. In addition, the use of ECLS to provide cardiovascular support during refractory electrical storm due to intrinsic cardiac disease such as Brugada or drug overdose has also been successfully used in those cases.

Conclusions

CA is a relatively common and lethal situation, with an estimated incidence in Europe of 375,000 a year. This implies that all emergency physicians will face many cardiac arrests in their careers. As professionals dedicated to emergencies, we need to be updated and know that, currently, the field of resuscitation is progressing continuously trying to find new techniques and resources to increase survival and improve neurological outcome in these patients.

The novelty of this case is the therapeutic use of ECLS and hypothermia as a bridge for a Class I antiarrhythmic drug toxicity with sustained ventricular fibrillation abnormally prolonged in time, with the help of LUCAS^{TM} device, trying to combine these new techniques and resources to ensure that a young man gets back home alive and with his higher brain functions preserved.

Conflict of interest

The authors declare no conflict of interest.

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