Brugada syndrome : clinical and pathophysiological aspects

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Lethal ECG Changes Hidden by Therapeutic Hypothermia

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Case Report

At 5:00 AM one morning in September 2005, a 42-year-old Caucasian man experienced cardiac arrest while asleep. His wife, woken by his distressed breathing, provided basic life support. His medical history was unremarkable and he used no medications. The first ECG, recorded by paramedics, showed ventricular fibrillation (VF), and, after defibrillation, sinus rhythm (83 beats per min) with widespread ST segment elevations, suggesting acute myocardial infarction (Figure, panel A). However, on admission to the hospital, primary coronary angiography and serial cardiac enzymes were normal. Serum electrolytes, echocardiography and cardiac MRI were also normal and the cause of his VF, therefore, remained unknown. Moreover, when he was cooled in the intensive care unit in order to preserve cerebral function after cardiac arrest ST segment elevations disappeared (Figure, panel B). ST segment elevations reappeared as he was re-warmed 1 day later after an uneventful cooling period (Figure, panel C). These ST elevations had a particular triangular shape with a high take-off point and descended smoothly into a negative T wave. They occurred in lead V1 and in leads overlying the right ventricular outflow tract, (i.e., cranial from V1 over the third intercostal space, [not shown]). This characteristic ST segment shape (so-called 'coved-type'[1]) in right precordial ECG leads, their strong temperature-sensitivity, and the classic clinical presentation (unexplained nocturnal VF in an otherwise healthy 40-year-old man with no structural heart disease), all fit the diagnosis of Brugada syndrome. ST segment elevations further increased during phlebitis-induced hyperthermia, and returned to normal at discharge (figure, panel D and E). The *SCN5A* gene, which encodes the cardiac sodium channel and is the only gene with generally accepted involvement in Brugada syndrome (mutations found in 20-30% of patients)[2, 3], was analyzed, but no mutations were found. However, this autosomal dominant inherited disease was proven when, upon family screening, the mother and two of the four siblings exhibited the typical ST segment elevations (≥ 2mm in at least 2 adjacent leads) during drug challenge with flecainide. He received an implantable cardioverter / defibrillator (ICD), and has made a full recovery without recurrence of VF at the last follow-up in August 2006.

Discussion

Brugada syndrome is a primary arrhythmia disorder, i.e., cardiac structural abnormalities are not detected using conventional cardiological tests [2]. In agreement with the functional basis of the disease, the ECG is highly variable, thereby confounding the diagnostic process. The signature ST segment elevations, harbingers of sudden death from VF, may increase during vagal stimulation [4] and hyperthermia [5]; their abolition by hypothermia is a new finding.

Reported Brugada syndrome-associated *SCN5A* mutations consistently result in reduced sodium current [6]. Accordingly, sodium channel blockers (ajmaline, flecainide), used in drug challenge, enhance these ST elevations or unmask them when they are not present at baseline [7]. The exact prevalence of Brugada syndrome, first reported in 1992 [8], is unknown. In some Southeast Asian regions it is endemic and a common killer among young men, second only to accidents [9]. In Europe, too, it is widely reported and an important cause of previously unexplained sudden death in young individuals [10]. Timely diagnosis by drug challenge after unexplained syncope and screening of relatives of known Brugada syndrome patients allows for preventive measures to avert SCD [11]. Our patient underwent comprehensive cardiological examination, but no drug challenge, following recurrent syncope 3 years earlier. Preventive measures include the avoidance of drugs which block the cardiac sodium channel (anti-arrhythmic drugs, some anti-depressants, anti-convulsants, anti-psychotics, and anesthetics) and the use of antipyretics during fever. In high-risk patients, prophylactic ICD implantation is recommended [2].

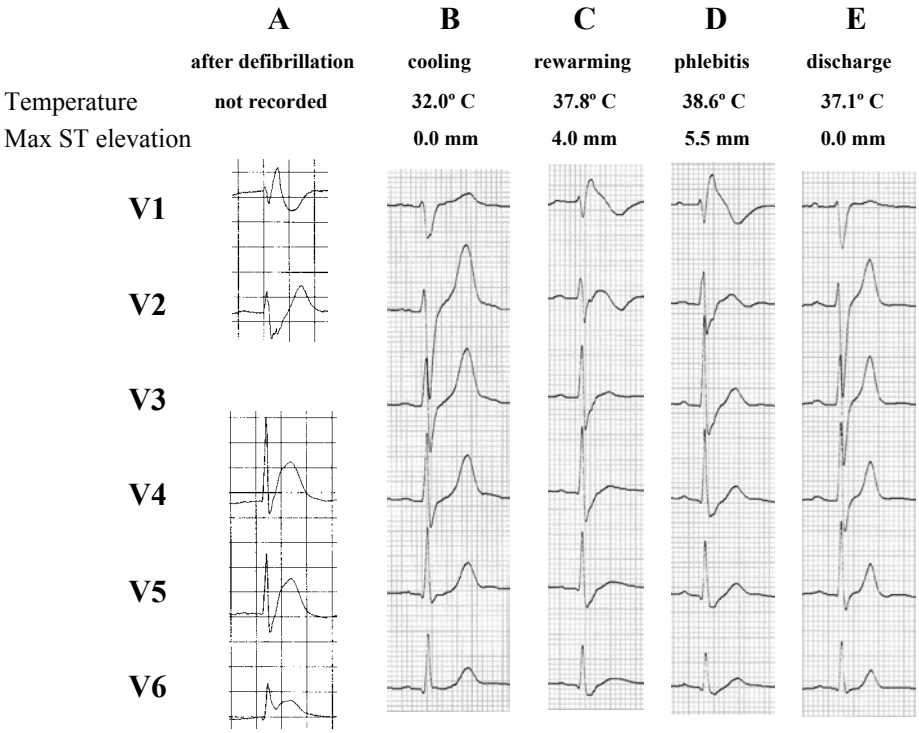

Figure: *ECG changes (lead V1-V6) from initial cardiac arrest to discharge.*

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