Commotio cordis and L-type calcium channel mutation: is there a link?

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Abstract

Commotio cordis is a rare phenomenon when ventricular fibrillation and sudden death occurs with a blunt, non-penetrating blow to the chest. Individual susceptibility to commotio cordis has been demonstrated in swine models, and might be present in humans as well. We report a case of commotio cordis in an adolescent with a heterozygous mutation on the gene CACNA1C, encoding for a L-type calcium channel expressed in the heart. This genetic mutation has been previously associated with a phenotype of long-QT syndrome, however this was not demonstrated in our patient despite extensive investigations. To the best of our knowledge, this is the first report of commotio cordis in which an ion-channel gene mutation involved in repolarisation abnormalities has been documented. This finding might corroborate the hypothesis that a genetic predisposition plays a role in the individual susceptibility to this rare cause of cardiac arrest.

Key words: commotio cordis; cardiac arrest; ventricular fibrillation; gene; sudden cardiac death.

Introduction

Commotio cordis is a rare phenomenon when ventricular fibrillation (VF) and sudden death occurs with a blunt, non-penetrating blow to the chest [1]. Most events are reported in young athletes (8-18 years old) who are struck by projectiles during sporting activities, such as balls or pucks [2]. Baseball, hockey and lacrosse are the most commonly involved sports in the USA [3]. Commotio cordis has also been reported during non-sporting activities, such as physical altercations. VF is induced by a mechano-electrical coupling causing triggered beats initiated by impact during the upslope of the T wave (window of vulnerability) [2].

Case study

Whilst playfully wrestling at school with a friend, a 14-year old male with no significant medical history was struck by a punch to his anterior chest. He initially felt dizzy and then lost consciousness in a few seconds. The teacher noticed him to be unresponsive and cyanotic. Cardiopulmonary resuscitation was started. He was connected to an external defibrillator and found to be in VF. Two shocks were required to restore spontaneous circulation and he was subsequently admitted to hospital. Extensive cardiac investigations, including electrocardiogram (ECG) (Fig. 1), echocardiogram, cardiac MRI, exercise stress test, 24-hour ECG Holter, and ajmaline test were unremarkable. There was no family history of sudden cardiac death. He underwent a genetic screening which documented a heterozygous mutation on the gene CACNA1C (variant Arg1906Gln), encoding for a L-type calcium channel expressed in the heart. This genetic mutation has been associated with long-QT syndrome (LQTS) [4];

however, no QT interval abnormalities were documented in our patient at baseline ECG (QTc 428 msec) and he also had a normal QT variability on a 24-ECG Holter and a normal QT response during an exercise stress test (Fig. 2). Family members were screened with ECG which was normal. He has remained under follow-up for a few years without experiencing any syncope or other cardiac symptoms, and with no ECG changes.

Discussion

Individual susceptibility to commotio cordis has been demonstrated in swine models. In a seminal study, Alsheikh-Ali et al [5] showed that the majority of animals were relatively resistant to VF, and only a very select minority were uniquely vulnerable. Interestingly, animals who were more susceptible to VF had significantly longer QRS and QTc intervals. This experimental data suggests that abnormalities in cardiac depolarisation/repolarisation are associated with an increased susceptibility to commotio cordis. An individual predisposition might also be present in humans. Maron and Link recently reported a case of a young patient who experienced two distinct episodes of commotio cordis, separated by one year [6].

To the best of our knowledge, this is the first report of commotio cordis in which an ion-channel gene mutation involved in repolarisation abnormalities has been documented. The CACNA1C encodes for the α-subunit of the L-type calcium channel which plays a critical role in the cardiac action potential, cellular excitability, excitation-contraction coupling, and regulation of gene expression [7-9]. Mutations of CACNA1C have been associated with LQTS-8 (Timothy syndrome) [4]. The Arg1906Gln variant of CACNA1C has been reported in one individual affected by LQTS; it has been hypothesized that this mutation could prevent the internalisation of

the channel, leading to an increased number of channels on the membrane, and a gain-of-function in Cav1.2 currents [7]. In an experimental model of commotio cordis, inhibition of L-type calcium channel with verapamil did not prevent VF induction [10]. However, this was a global effect of verapamil which could have neutralized the influence of Ca^{2+} channel effects promoting homoegenous repolarization patterns. It is recognized by ECG imaging studies that there can be marked heterogeneities in repolarization over the epicardium in LQTS [11]. Therefore, it is conceivable that a stretch induced triggered beat either promoted wavebreak on the borderzone of a repolarisation wavefront in a region of increased vulnerability caused by heterogenous repolarisation or the myocardium was more likely to generate triggered beats due to Ca^{2+} overload. In conclusion, our anecdotal finding might corroborate the hypothesis that a genetic predisposition plays a role in the individual susceptibility to commotio cordis.

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Legends to figures

Figure 1. Twelve-lead electrocardiogram (speed 25 mm/sec)

Figure 2. Physiological QT response during exercise stress test (lead II, speed 25 mm/sec)