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Brugada syndrome and calcium channel mutation in a patient with congenital deaf mutism

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ABSTRACT

To the best of our knowledge, for the first time in the literature, we described a congenitally deaf-mute patient with Brugada syndrome (BrS) in whom a mutation in L-type Ca^{+2} channel [CACNA1C ($Ca_v1.2\alpha1$)] was identified.

Letter to the Editor,

A 28-year-old congenitally deaf-mute male patient admitted to our emergency room with the compaint of cardiac syncope for the first time. His initial evaluation including vital signs and physical examination were normal. His past medical history was unremarkable including smoking, illicit drug use and any other disease conditions. He has a congenital sensorineural hearing loss and mutism. Family history revealed a sudden death in his father at the age of 38 years old with unknown etiology. His electrocardiography (ECG) on admission showed a sinus rhythm (60 bpm) with incomplete right bundle branch block, normal QT interval and no ischemic changes (Fig. 1A). Chest-X-ray, echocardiography and laboratory tests including cardiac panel were also in normal limits. He has been consulted us for further cardiac evaluation. Because of his complaint of cardiac syncope and the presence of incomplete RBBB on initial ECG, we aimed to exclude inherited arrhythmic syndromes like Brugada syndrome (BrS). A 24-h Holter monitorization demonstrated no arrhtyhmic episodes. Cardiac magnetic resonance imaging (MRI) has been performed to exclude arrhythmogenic right ventricular dysplasia. In addition, resting ECGs were similar after placement of precordial leads V1-2 in the standard vs higher position (second intercostal space) in regard to ST segment and T wave changes. Therefore, we performed the ajmaline challange test (1 mg/kg ajmaline i.v. in 5 min) because of the suspicion for BrS. The serial ECG 5 min after ajmaline administration demonstrated typical coved-shape ST segment elevation in leads V1-3 (type 1 Brugada pattern) (Fig 1B). Thus, the patient has been diagnosed as BrS. Because of the history of cardiac syncope, he underwent successful implantation of an implantable cardioverter defibrillator (ICD) and discharged uneventfully. Furthermore, we consulted him to our genetic outpatient clinic for detailed analysis and counseling because of concomitant presence of BrS and congenitally deaf-mute condition. Genomic DNA analysis from peripheral blood lymphocytes of the patient revealed a mutation in L-type Ca^{+2} channel [CACNA1C (Cav1.2α1)]. After 4th months of discharge, he admitted to emergency room with recurrent ICD shocks and ICD interrogation revealed a 3 appropriate shocks for sustained ventricular tachycardia (VT). Thus, quinidine therapy was initiated and he was stable without any shocks/episodes for 15 months.

Brugada syndrome is known as one of the more common forms of familial arrhythmic syndromes and characterized by a dynamic or persistent ST-segment elevations in the precordial leads V_{1-3} and an enhanced risk of syncope and sudden cardiac death in young adults without structural heart disease [1–3]. As an inherited arrhythmia syndrome, BrS is inherited via an autosomal dominant mode of transmission. Among several responsible genes identified so far, either a reduced inward sodium or calcium current or an increased in one of the outward potassium currents has been

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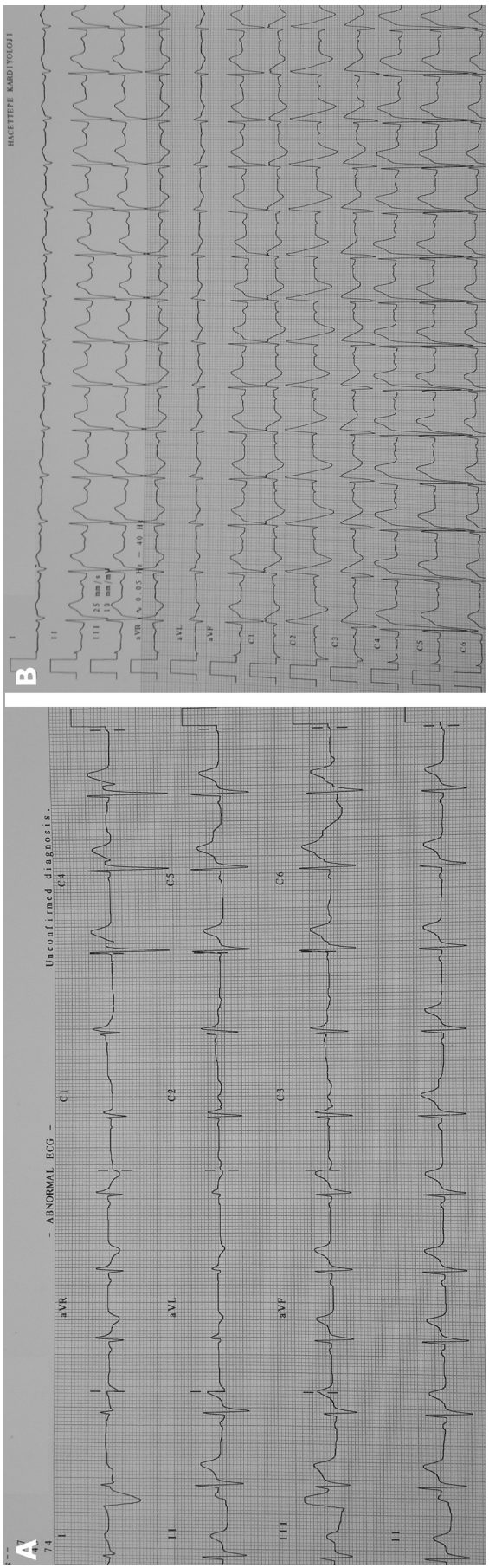

Fig. 1. Electrocardiography (ECG) on admission showing normal sinus rhythm (60 bpm) with incomplete right bundle branch block, normal QT interval and no ischemic changes (A). The serial ECG 5 min after ajmaline administration demonstrated typical coved-shape ST segment elevation in leads V_{1-3} (type 1 Brugada pattern) during ajmaline challange test (B).

shown to be associated with the BrS phenotype [1]. Congenital deaf and mute state may also be associated with various channel mutations including repolarizing potassium channels, acalcium and sodium channels and connexin channels [4–6]. It has been previously reported that L-type Ca^{+2} channelopathy of gain or loss-of-function mutations in the CACNA1C ($Ca_v1.2\alpha1$) may cause Timothy and Brugada syndromes [7,8]. Also mutations in the CACNA1D ($Ca_v1.3\alpha1$) with low prevalence most commonly result in lethal dysfunction and presents with congenital cardiac (sinoatrial node dysfunction) and auditory (severe to profound deafness) phenotype [6]. Our patient is congenitally deaf and mute and also diagnosed as BrS. His genetic analysis revealed a mutation in the CACNA1C ($Ca_v1.2\alpha1$) gene. Although in a previous study by Antzelevitch et al. [8] a significant relationship between CACNA1C ($Ca_v1.2\alpha1$) mutation and BrS has been identified, patients with BrS demonstrated a shorter QT interval than normal. They also did not report any auditory or speech abnormality among study population. However, our patient have had a congenital deaf and mute condition and showed a normal QT interval on admission. To our knowledge, this is the first report in the literature showing such an association between congenitally deaf and mute state and BrS in a patient with a mutation in CACNA1C ($Ca_v1.2\alpha1$) gene. However, deaf-mute condition could also be a coincidence rather than causative in our case. Thus, further studies are needed to identify exact relation of BrS with congenitally deaf and mute state and their association with CACNA1C ($Ca_v1.2\alpha1$) gene and highlight to screen congenitally deaf and mute patients for the presence of concomitant BrS.

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Conflict of interest

None declared.

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