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Incessant left ventricular tachycardia of unusual etiology

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ABSTRACT

Apart from Coronary artery disease, left ventricular tachycardia may result from cardiac sarcoidosis, left ventricular tumor, chagas disease and idiopathic left ventricular tachycardia. We report a rare case of incessant left ventricular tachycardia resulting from left dominant arrhythmogenic cardiomyopathy.

1. Case report

A 40 years male patient presented to our institute with history of palpitation for the past 10 days. Electro cardiogram (ECG) showed monomorphic ventricular tachycardia (VT) of right bundle branch block (RBBB) morphology (Fig. 1). The VT was resistant to electrical cardioversion was terminated after 12 hours of intravenous Amiodarone and phenytoin. ECG in sinus rhythm was normal with a corrected QT interval of 420 ms. He gave history of recurrent episodes of palpitation in past. He was diagnosed to have idiopathic left ventricular tachycardia and underwent radiofrequency ablation for the same six months earlier. Serum electrolytes and cardiac biomarker (Troponin T) were within normal range. Echocardiography showed normal bi-ventricular function. His coronary angiography showed normal coronary arteries. Contrast enhanced cardiac MRI (CMRI) showed abnormal sub-endocardial and mural late gadolinium enhancement (LGE) with in apical inferior and apical septal wall of left ventricle (Fig. 2). On the back ground of CMRI finding he was investigated for sarcoidosis. His angiotensin converting enzyme (ACE) level was within normal range, contrast-enhanced computed tomography (CT) chest scan was normal and Mantoux test showed 20 mm × 20 mm induration after 72 hours. The QuantiFERON-TB Gold test (QFT-G) was within normal range. Endomyocardial biopsy from right side of inter-ventricular septum showed myocytes loss and fatty replacement (Fig. 3). A diagnosis of left dominant arrhythmogenic cardiomyopathy (LDAC) was made. Considering the genetic basis of LDAC, patient was subjected to Genetic analysis. Genomic DNA was subjected to exome sequencing by Next Generation sequencing (NGS) technique. Genes responsible for arrhythmogenic cardiomyopathy were analysed for sequence variations. The individual harboured a variation (p.Thr277Ser) caused by a substitution (c.829A > T) in exon 10 of the TMEM43 gene. His mother did not have this variation by mutation analysis study and father was not available for gene testing.

2. Discussion

Usual causes of left ventricular tachycardia include coronary artery disease, cardiac sarcoidosis, left ventricular tumor, chagas disease and idiopathic left ventricular tachycardia. Arrhythmogenic cardiomyopathy usually presents as ventricular tachycardia of right ventricular origin because the pathogenic process classically involves right ventricle. Although concurrent left ventricular involvement along with right ventricle occurs in 75% cases of advanced disease [1], isolated LV involvement is rare. In a study of 200 patients 5% patients had isolated left ventricular involvement [2]. About 75% of Left dominant Arrhythmogenic Cardiomyopathy (LDAC) presents with ventricular arrhythmia of RBBB morphology [3,4]. Most common baseline ECG finding in LDAC patients is T wave inversion in (infero) lateral Leads in absence of heart failure and left

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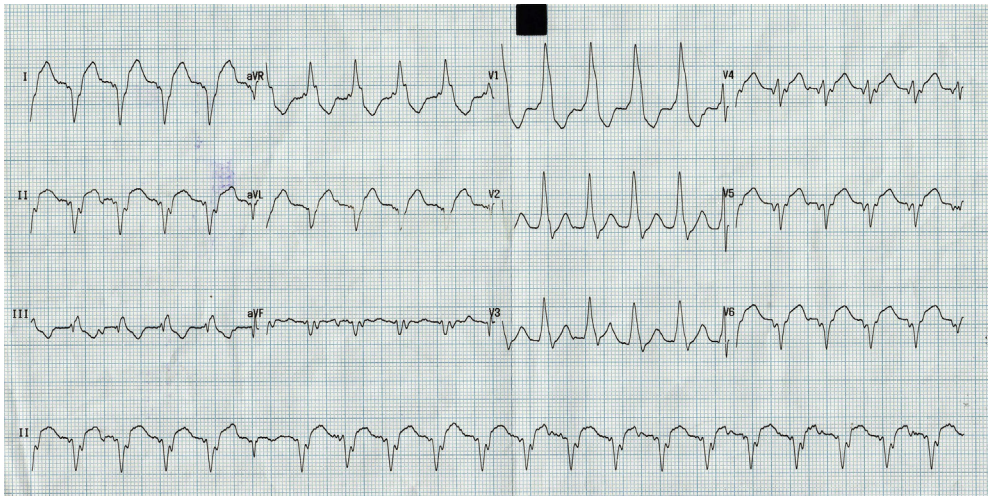

Fig. 1. ECG showing monomorphic Ventricular tachycardia of Right Bundle branch Block (RBBB) morphology.

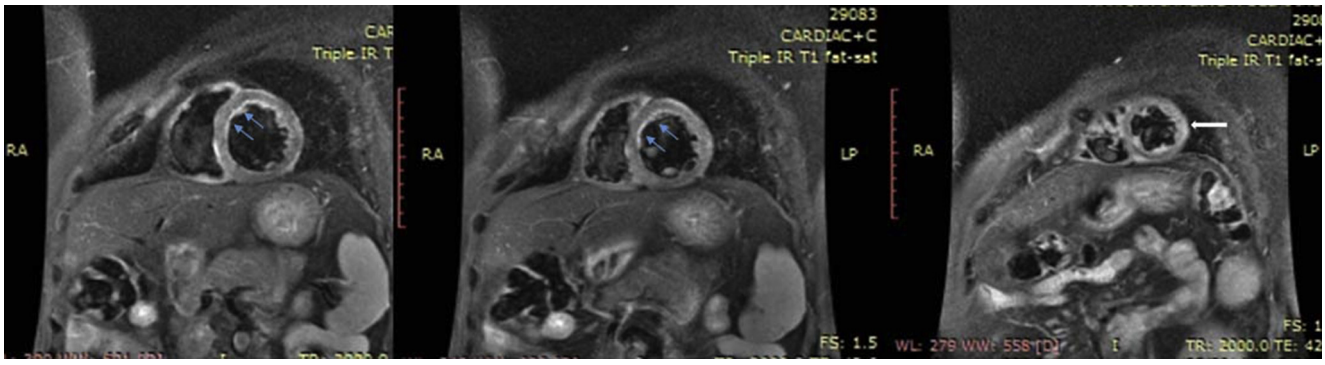

Fig. 2. Contrast enhanced cardiac MRI (CMRI) showed abnormal sub-endocardial (arrows) and mural (Block arrow) late gadolinium enhancement (LGE) in Left Ventricle.

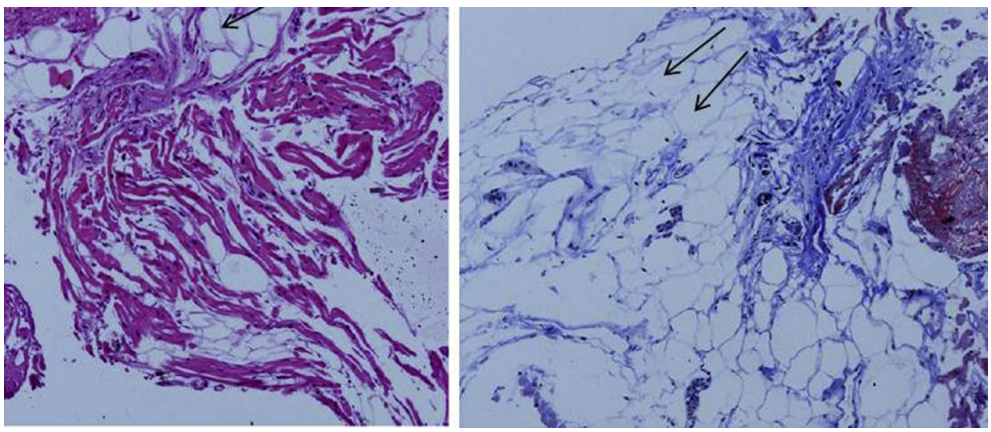

Fig. 3. Endomyocardial biopsy from right side of inter-ventricular septum showed myocytes loss and fatty replacement.

ventricular hypertrophy [4], in our case baseline ECG was normal. Cardiac MRI study demonstrates LV dilatation/dysfunction, aneurysm formation, regional wall motion abnormality and late gadolinium enhancement (LGE) with no or minimal RV involvement. Late gadolinium enhancement (LGE) distribution classically affects subepicardial or midwall region [3]. Inter ventricular septum (IVS) is rarely involved in advanced ARVC with LV involvement whereas more than 50% patients with LDAC have septal involvement [4]. Like ARVC, LDAC is also a genetically determined disease affecting heart muscle. The disease is a genetically heterogeneous and is most commonly inherited in an autosomal-dominant fashion. Mutation of desmosomal proteins (Desmoplakin, desmoglein-2 and plakophilin-2) has been reported in patients with LDAC [2,4]. The desmosomal model of arrhythmogenic cardiomyopathy suggests that mutations in desmosomal genes may compromise either intercellular adhesion or intermediate filament function or both.

Consequent myocyte loss may be accompanied by an inflammatory response and is followed by repair with fibrous or fibro fatty tissue [5]. In our patient, a variation in the sequence of TMEM 43 gene (p.Thr277Ser) was noted. TMEM43, also known as LUMA, is a highly conserved inner nuclear membrane (INM) protein [6,7]. Mutations in this gene are a relatively rare cause of ARVC. The mechanism by which TMEM 43 mutations cause ARVC is still unclear. It has been hypothesized that mutant TMEM43 protein would disrupt structure and function of desmocollin-2, desmoglein-2, desmoplakin, and junctional plakoglobin, leading to ARVC [6]. Significance of p.Thr277Ser substitution is unclear. This variation has been identified previously, in a 16 year old male patient with ARVC [8]. Two out five in-silico prediction tools suggested that The Thr277 residue is well conserved and the change is predicted to be damaging and occurs in an amino acid that is evolutionarily conserved across mammalian species as well as D. Melanogaster [8]. Also, the variant has been identified in one of 427 control individuals [9]. Protein modelling of the mutant protein to check the deleterious effect of the sequence variation was not possible in view of lack of availability of structure of the wild type protein in the database. Any homologous protein structure with up to 80% homology with TMEM 43 protein was also not available. Thus, it is uncertain if the c.829A [T (p.T277S) variant is related to his ARVC presentation. To conclude we report a rare case of incessant left ventricular tachycardia due to LDAC associated with variation in TMEM43 gene.

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