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Sudden cardiac death prevention in an Emery–Dreifuss muscular dystrophy patient

Running title: ICD implantation in a patient with EDMD

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Main text

There are clinical challenges for young patients with Emery–Dreifuss muscular dystrophy (EDMD), mainly involving optimal timing and lead position for implantable cardioverter-defibrillator (ICD) insertion for the primary prevention of sudden cardiac death (SCD).

Our patient was a 17-year-old girl with gait disturbance and ankle joint contracture since age one. By two years of age, a muscle biopsy performed revealed dystrophic change with mild mononuclear cell infiltration (Fig. 1a)[1]. Genetic analysis revealed a c.94_96 del mutation in exon 1 of the lamin A/C gene. Her first cardiac involvement was prolongation of PR interval on electrocardiography, which progressed over time and first-degree atrioventricular block (AVB) was recognized at the age of 11. In addition, late gadolinium enhancement (LGE) on magnetic resonance imaging (MRI), which was not recognized initially, was detected. We attributed this to myocardial damage progression and decided that it was preferable to prepare for not only conduction impairment but also lethal arrhythmias. By the age of 13, couplet (premature ventricular contractions) was recognized. However, there was no consensus on when ICD should be implanted until non-sustained ventricular tachycardia (NSVT) occurred at the age of 15 (Fig. 1b). The combination of NSVT and non-missense mutations indicated ICD insertion according to the conventional risk stratification method but was not applicable to patients under 16 years of age[2]. Therefore, we decided to insert ICD with an expanded interpretation. The patient achieved

maximum growth in height, 155 cm (Fig. 1c), and underwent transvenous insertion of a dual-chamber ICD. Although LGE presence in the right ventricular wall could not be evaluated due to limitations of image quality, most of the right atrium and ventricle had low endocardial voltage during ICD insertion. Thus, ICD lead had to be placed in a relatively high voltage area and could not be placed in the right ventricular apex. The device was programmed with two zones; a ventricular fibrillation zone with the lower detection rate of ≥200 bpm and a ventricular tachycardia zone with a rate ≥170 bpm. In the ventricular fibrillation zone, anti-tachycardia pacing during charging and subsequent shocks were included. At the age of 17, she developed ventricular fibrillation while talking with a friend at school. She had an atrial sensed–ventricular paced rhythm of 70 bpm due to advanced AVB before that episode. Initially, sporadic premature ventricular contraction occurred, and subsequently ventricular fibrillation lasted for about 27 seconds at a rate of about 230 bpm. 35.5 J shock was then delivered, terminating the episode. The interval from the episode to echocardiography evaluation was short, but echocardiography showed no decline in cardiac function with ejection fraction of 56% (Fig. 1b).

PR interval prolongation was recognized long before NSVT occurred in our patient. The latest risk prediction model for life-threatening ventricular tachyarrhythmias incorporated PR interval as a risk factor[3]. Applying this model to our patient showed that the risk at the age of 11, when first-degree AVB was recognized, was 14.3% per 5 years, beyond the indication line for ICD insertion,

but this model was also not applicable to those under the age of 16. In addition, it was reported that, in adult patients with PR interval prolongation, LGE was detected in 80% of patients with ventricular arrhythmia and 0% without ventricular arrhythmia[4]. Our patient indicated that presence of LGE with PR interval prolongation may be a risk factor for development of fatal arrhythmias even in children. However, it was reported that right ventricular pacing in patients with LGE presence tended to reduce cardiac function[5]. Therefore, it was necessary to monitor cardiac function transition after ICD insertion in patients with EDMD, who were prone to AVB progression. In addition, ICD insertion in endocardial low-voltage areas, which can cause pacing failure, should be avoided. It is presumed that the area of LGE is low-voltage one as in non-ischemic cardiomyopathy, but if presence of LGE in the right ventricle cannot be identified as in our patient, a voltage mapping study in advance may help determine the optimal pacing site.

Until risk prediction models for children have been established, if NSVT is observed in patients under the age of 16, LGE on MRI concomitant with PR interval prolongation may be an indication for ICD implantation for primary prevention of SCD.

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Consent to participate: The study participant provided informed consent.

Author contributions: All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by HY, GI, HK, and IN. The first draft of the manuscript was written by HY, and all authors commented on previous versions of the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Figure Legends

Fig 1a

Mild inflammatory cellular infiltration observed with hematoxylin and eosin staining.

Fig 1b

Timeline of events leading to appropriate discharge of the cardioverter-defibrillator

Abbreviations: ECG, electrocardiogram; EF, ejection fraction; ICD, implantable cardioverter-defibrillator; LGE-MRI, late gadolinium enhancement-magnetic resonance imaging; UCG, Ultrasonic echocardiography

Fig 1c

Growth curve showed that the patient achieved almost maximum growth in height at 14 years of age.

Fig. 1a

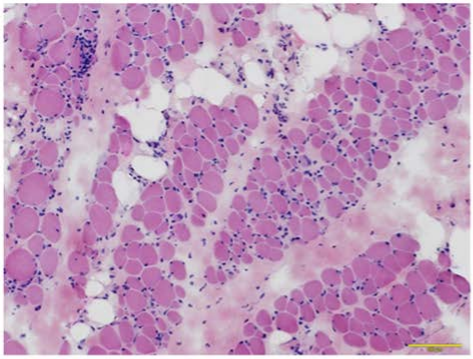

Fig. 1c

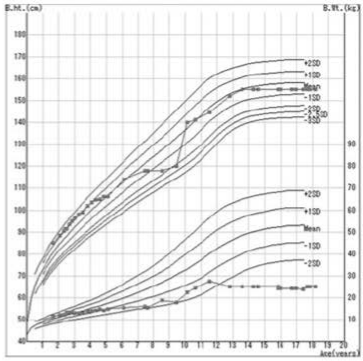

Fig. 1b