Challenges in the primary prevention of sudden cardiac death in hypertrophic cardiomyopathy in the young

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Abstract

A case of hypertrophic cardiomyopathy in the transition from childhood to adulthood, which was low-risk by the conventional risk assessment model, medium-risk by the adult risk prediction model, and high-risk by the pediatric risk prediction model was inserted an implantable cardioverter-defibrillator. Three years post-implantation, the patient was resuscitated with an appropriate discharge of cardioverter-defibrillator.

Keywords

implantable cardioverter-defibrillator, hypertrophic cardiomyopathy, late gadolinium enhancement-MRI, primary prevention of sudden cardiac death, risk prediction model

Introduction

Hypertrophic cardiomyopathy is a well-known cause of sudden cardiac death in the young. Therefore, the primary prevention of sudden cardiac death is imperative. It is important to make a clear distinction between candidates and non-candidates for the primary prevention of sudden cardiac death. The risk of sudden cardiac death can now be calculated probabilistically using risk calculation models for adults and children. However, it remains a challenge to distinguish between candidates and non-candidates for the primary prevention of sudden cardiac death. Herein, we present a case of hypertrophic cardiomyopathy in the transition from childhood to adulthood where we contemplated inserting an implantable cardioverter-defibrillator.

Case Report

The patient was a 20-year-old male with hypertrophic cardiomyopathy whose electrocardiogram showed an abnormal T-wave. He was diagnosed at 6 years of age by echocardiography. A p.Ala63Val mutation in the Tropomyosin alpha-1 (TPM1) gene, which is one of the sarcomere genes, was detected through genetic analysis of the patient. The patient's family history revealed that his elder brother, father, and grandmother also had hypertrophic cardiomyopathy and his paternal uncle died suddenly; however, it is unclear whether the death was associated with hypertrophic cardiomyopathy. The elder brother had an episode of syncope at 18 years of age while running, but was resuscitated using an automated external defibrillator by a bystander.

Before the insertion of the implantable cardioverter-defibrillator, the patient had none of the five major classical risk factors (non-sustained ventricular tachycardia, a maximum left ventricular wall thickness ≥30 mm or a Z-score ≥6, family history of sudden cardiac death associated with hypertrophic cardiomyopathy, unexplained syncope, and abnormal blood pressure response to exercise) associated with sudden cardiac death[1], except the elder brother's near-miss event, which was considered a possible risk factor. Thus, the patient was deemed a low-risk case. In contrast, the patient's late gadolinium enhancement-MRI results showed an increasing late enhancement area of 1% to 16% of left ventricular mass over two years between ages 10 and 12. We considered this an indication of increased risk. However, to reduce the probability of complications due to implantable cardioverter-defibrillator insertion, we decided to wait until growth slowed down. When the patient turned 16 years of age, we applied the risk prediction model from the 2014 European Society of Cardiology for hypertrophic cardiomyopathy over 16 years of age at the time[2], and the risk of sudden cardiac death was assessed at 4.8 % per 5 years, which means that implantable cardioverter-defibrillator insertion was still an option. Ultimately, although aggressive conclusion that should be inserted an implantable defibrillator was not obtained, we obtained informed consent from the patient and his family and implantable cardioverter-defibrillator insertion was planned for the primary prevention of sudden cardiac death[3]. The patient underwent the transvenous insertion of a dual chamber implantable cardioverter-defibrillator at 17 years of age after achieving maximum

growth in height. The device was programmed with two zones; a ventricular fibrillation zone with the lower detection rate of ≥220 bpm and a ventricular tachycardia zone with a rate ≥180 bpm. In the ventricular tachycardia zone, two sequences of anti-tachycardia pacings and subsequent shocks were included. Three years later, the patient experienced a syncopal episode due to a ventricular tachycardia attack when he was having lunch at the university cafeteria. He had a sinus rhythm of 94 bpm before this episode. Initially, monomorphic ventricular tachycardia with rates between 160 and 180 bpm occurred and sustained for approximately 4 minutes. Subsequently, it accelerated above 180 bpm and anti-tachycardia pacing therapies were given, which failed to terminate ventricular tachycardia. 21 J shock was then delivered, which terminated the episode. However, polymorphic ventricular tachycardia with a rate of about 200 bpm recurred immediately, and 41 J shock was delivered, which restored sinus rhythm.

Discussion

In this case, the necessity of inserting the implantable cardioverter-defibrillator could not be confirmed before the procedure. Before the publication of the 2014 European Society of Cardiologist risk prediction model, this case was assessed as low-risk, and inadequate evaluation was attributed to the lack of weighting of risk factors. Since its publication in 2014, risk factors have been weighted. However, this still cannot be applied to patients under 16 years of age.

Ultimately, evaluating our patient at 16 years of age using this model was not sufficiently valid. It has been known that the risk prediction model has a lower sensitivity and, as a result, misidentified patients who later experienced a sudden cardiac death event as low risk. In fact, in the American Heart Association Scientific Sessions 2019, the Tufts hypertrophic cardiomyopathy institute reported a sensitivity of 50% when using the risk prediction model[4]. Moreover, a validation study of the risk prediction model in adult Japanese cases showed an even lower sensitivity of 32% than Western cases[5]. In our case, implantable cardioverter-defibrillator insertion was considered based on changes in the findings of late gadolinium enhancement-MRI. However, after the procedure in our patient, two new pediatric risk prediction models were published. Based on the risk prediction model proposed by Norrish et al.[6], the risk of sudden cardiac death in our patient at 16 years was assessed at 9.4 % per 5 years, which is beyond the indication line for implantable cardioverter-defibrillator insertion. Furthermore, applying the latest risk prediction model applicable to those under the age of 18 reported by Anastasia et al.[7], the risk at the age of 16 was 8.9 % per 5 years, which is also beyond the indication line for implantable cardioverter-defibrillator insertion. Afterthought, it can be said that the new pediatric risk prediction model was able to perform a valid risk assessment in this case.

Based on the above, in the case of hypertrophic cardiomyopathy in the transition from childhood to adulthood, if the risk prediction model is within the age range that can be used, not only the 2014

European Society of Cardiology risk prediction model but also the recent pediatric risk prediction models should be used to consider the indications for implantable cardioverter-defibrillator insertion. For this purpose, it is necessary to hurry the validation study in Japanese cases.

Conclusion

There are still challenges in assessing the risk of sudden cardiac death in hypertrophic cardiomyopathy in the young. Although new risk assessment models are promising, robust validation of these new risk assessment models in Japanese cases is needed.

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Conflicts of Interest: None.

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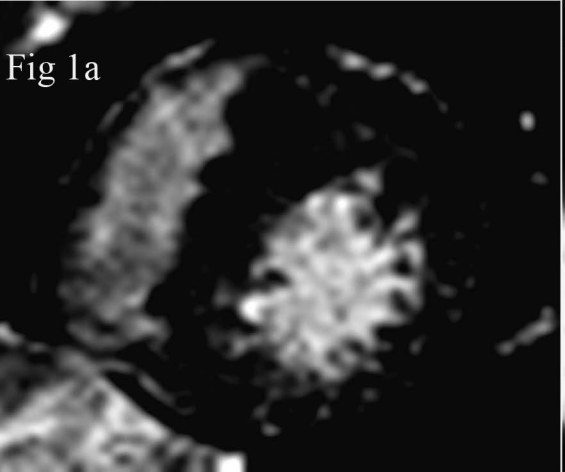


Fig 1a

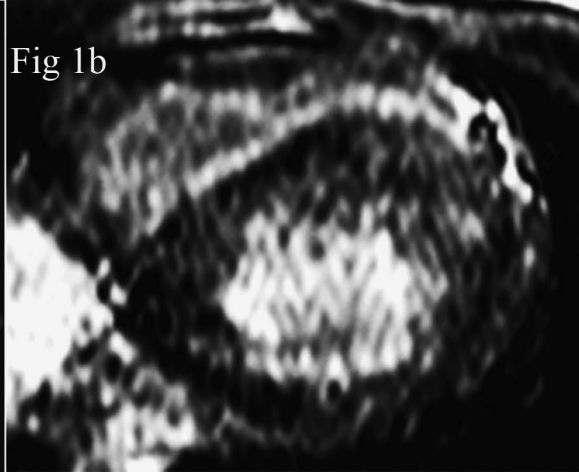


Fig 1b

Fig 2a

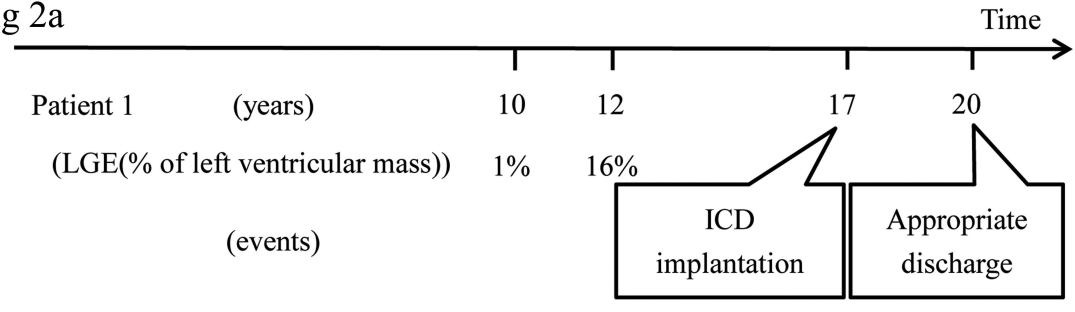
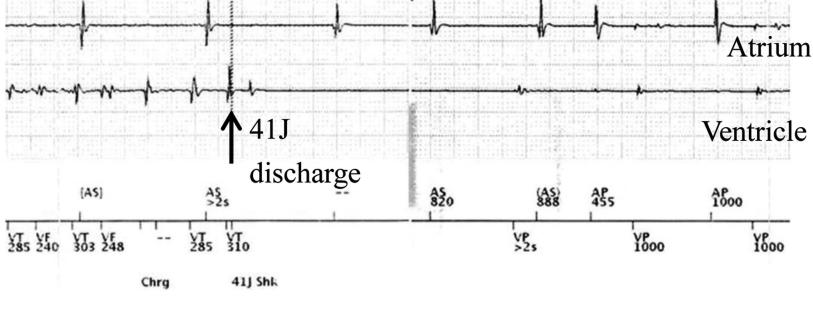

Time
Patient 1
(years)
10
12
17
20
(LGE(% of left ventricular mass))
1%
16%
(events)
ICD implantation
Appropriate discharge

Fig 2b


Atrium
Ventricle
41J discharge
[AS]
AS >2s
AS 820
(AS) 888
AP 455
AP 1000
VT 285
VF 240
VT 303
VF 248
VT 285
VT 310
VP >2s
VP 1000
VP 1000
Chrg
41J Shk