CASE REPORT

Prediagnostic electrocardiographic and echocardiographic findings of biopsy-proven hypertrophic cardiomyopathy

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Abstract
We present two cases of biopsy-proven hypertrophic cardiomyopathy (HCM). Both cases showed abnormal electrocardiographic (ECG) findings more than 8 years before diagnosis. A 16-year-old healthy male experienced a rescued cardiac arrest. Another male adolescent showed abnormal Q wave and thickened ventricular wall at 15 years old. Retrospective analyses of ECGs performed at 6 years old indicated abnormal ECG findings. However, the diagnosis was normal because no ventricular wall thickening was present in echocardiography. For early diagnosis of HCM to prevent sudden cardiac arrest or death, it is essential to establish ECG and echocardiographic criteria to screen HCM in the young.

KEYWORDS
biopsy, echocardiography, electrocardiography, gene mutation, hypertrophic cardiomyopathy

1 | INTRODUCTION

HCM is a leading cause of sudden cardiac death (SCD) or out-of-hospital cardiac arrest in the young. Diagnosis of HCM is made when the left ventricular wall (LVW) thickness is ≥15 mm in one or more left ventricular myocardial segments in adults.1 Criteria of echocardiographic diagnosis for children and adolescents are not fully established, except for first-degree relatives of patients with HCM and the presence of otherwise unexplained LVW thickness ≥13 mm.1 Standard 12-lead ECG shows a variable combination of left ventricular hypertrophy, ST and T wave abnormalities, and pathological Q waves.1 However, appearance of these abnormalities before diagnosing HCM is unclear. We present prediagnostic ECG and echocardiographic findings in two adolescents with biopsy-proven HCM.

2 | CASE REPORT

2.1 | Patient 1

A 16-year-old adolescent with no family history of cardiomyopathies or SCD experienced a witnessed sudden cardiac arrest while playing soccer. Immediate cardiopulmonary resuscitation was initiated, and spontaneous circulation returned after discharge of an automated external defibrillator. HCM was suspected because of the presence of cardiac arrest, his ECG findings (Figure 1A) and echocardiographic findings (Figure 1B). His echocardiography at admission to our hospital showed a thickened LVW. To confirm the diagnosis, endomyocardial biopsy from the right ventricle was performed and it showed findings suggesting HCM (Figure 1C). His genetic testing showed a homozygous

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missense mutation, p.R130C (c.388C>T), in TNNT2 encoding troponin T in which mutations are associated with HCM. An implantable cardioverter defibrillator (ICD) was implanted. In retrospective analyses of ECGs at a school-based screening program, his ECG at 6 years old showed right ventricular hypertrophy and incomplete right bundle branch block (Figure 1A). However, he was diagnosed as normal because echocardiography showed no congenital heart diseases or LVW thickening. His ECG at 12 years old showed similar findings, but further workups were not performed because his previous echocardiography showed no abnormalities. After ICD implantation at 16 years old, he is well with medication and no appropriate ICD discharges.

2.2 | Patient 2

A 12-year-old adolescent was referred for evaluation of abnormal Q waves in leads V1-V2 (Figure 2A) in ECG at a school-based screening program at the 7th grade. He was asymptomatic and had no family history of cardiomyopathies or SCD. In retrospective analysis of a school-based screening program, his ECG at 6 years old showed abnormal Q waves. Further examination showed no congenital heart diseases or LVW thickening (6.3 mm, Figure 2B). Echocardiography at the first visit showed an LVW thickness of 8.6 mm. He was followed approximately within 6-month intervals. Thirty months after the first visit, his ST-T morphology in leads V4-V6 dramatically changed, and the LVW thickened to 11.9 mm. HCM was highly suspected and left ventricular endomyocardial biopsy was performed; it showed findings compatible with HCM (Figure 2C). His α-galactosidase A activity was normal (10.93 nanomoles per hour per ml; normal range 3.6–17.6 nanomoles per hour per mL). A beta-blocker was initiated and he is well with medication. We performed genetic analysis, but we did not identify any causative mutation of HCM including alpha galactosidase gene associated with Fabry disease.

3 | DISCUSSION

The European Society of Cardiology guideline for HCM recommends a diagnostic criterion for childhood HCM: an LVW thickness greater than the mean values plus two standard deviations. This criterion implies that 2.5% of the general population might be diagnosed with HCM. The prevalence of HCM in childhood is estimated to be 2.9 per 100 000. Therefore, the diagnostic criterion for first-degree relatives of patients with HCM is generally applied in school-based screening programs in Japan. Findings in our two patients indicate
that the changes in myocardial tissue have already presented before the appearance of hypertrophic changes in echocardiography. High amplitude of R wave plus S wave (R + S wave) in case 1 and abnormal Q wave in case 2 were present in their 1st grade's ECGs. The amplitude of R + S wave in V2 and V3 (6.2 and 5.2 mV respectively) in case 1 is above 99th percentile in normal 1st grade population.3 Multiple studies have demonstrated the relationship between ECG abnormalities and HCM.4,5 Therefore, abnormal ECG finding should be regularly followed up because appearance of echocardiographic findings may follow those of ECG findings in HCM. For early diagnosis of HCM to prevent sudden cardiac arrest or death, establishing an ECG criterion to screen HCM and echocardiographic criterion to diagnose HCM in children and adolescents is required.

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CONFLICT OF INTEREST
Authors declare no conflict of interests for this article.

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REFERENCES

1. Elliott PM, Anastasakis A, Borger MA, et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J. 2014;35(39):2733–79.

2. Norrish G, Cantarutti N, Pissaridou E, et al. Risk factors for sudden cardiac death in childhood hypertrophic cardiomyopathy: a systematic review and meta-analysis. Eur J Prev Cardiol. 2017;24(11):1220–30.

3. Yoshinaga M, Iwamoto M, Horigome H, et al. Standard values and characteristics of electrocardiographic findings in children and adolescents. Circ J. 2018;82(3):831–9.

4. Brothers MB, Oster ME, Ehrlich A, et al. Novel electrocardiographic screening criterion for hypertrophic cardiomyopathy in children. Am J Cardiol. 2014;113(7):1246–9.

5. Delcrè SD, Di Donna P, Leuzzi S, et al. Relationship of ECG findings to phenotypic expression in patients with hypertrophic cardiomyopathy: a cardiac magnetic resonance study. Int J Cardiol. 2013;167(3):1038–45.

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