Case Report

Qin Tao, Junhua Yang, Weili Cheng, Shenghua Yu, Xu Fang, Pingping He, Yuqing Zhang*

A novel TNNI3 gene mutation (c.235C>T/ p.Arg79Cys) found in a thirty-eight-year-old women with hypertrophic cardiomyopathy

1 Introduction

Characterized by idiopathic hypertrophy, especially the interventricular septum (IVS), hypertrophic cardiomyopathy (HCM) is one of the most commonly inherited cardiovascular diseases. Family history of about half of the patients are positive for HCM. Family HCM often presents an autosomal dominant (AD) pattern of inheritance, which is due to mutation of the genes encoding sarcomeric proteins. Until now, there are approximately 450 point mutations in 13 genes contributing to HCM, among which, beta-myosin heavy chain (MYH7), cardiac troponin I (TNNI3), myosin binding protein C (MYBPC3), cardiac troponin T (TNNT2) are most common [1]. Families with various mutations of HCM exhibit a variety of phenotypes and prognosis. Recent evidence showed that the mutations of responsible gene may not be related to the disease phenotype, or the gene mutation is not associated with clinical presentation [2, 3].

Investigation of genetic basis of HCM is contributable to deeply understand the pathogenesis of cardiac hypertrophy and may improve the prevention, diagnosis, treatment of the disease. Here we report a case of thirty-eight-year-old women with HCM who is a carrier of a novel point mutation in TNNI3 and screen the gene of her family at the same time. We are carefully following up with this patient and her family to observe the prognosis of HCM caused by this mutation.

2 Case report

A thirty-eight-year-old woman was admitted to our hospital due to palpitation and chest distress. She was in good health before without high blood pressure or diabetes. The clinic twelve-lead electrocardiography (ECG) indicated sinus rhythm with ST-T segment change, PR interval was 160ms, QT interval was 447ms, QRS width was 100ms, and Sokolow index was 67mm. Therefore, it is recommended to further perform the echocardiogram. Transthoracic
A novel TNNI3 gene mutation (c.235C>T/ p.Arg79Cys) found in a thirty-eight-year-old women...  

were searched in the proband and a heterozygous mutation (c.235C>T/ p.Arg79Cys) in TNNI3 for cardiac troponin I was identified. Up to now, only 5 mutations in TNNI3 associated with HCM were reported, namely, c.37C>T/ p. Arg13Cys, c.422G>A/ p. Arg141Gln, c.433C>T/ p. Arg145 Trp, c.434G>A / p. Arg145Gln, c.470C>T/ p.Ala157 Val [4]. We report a new mutation (Figure 1).

No one died suddenly in the family (Figure 2) and we suggest that her immediate relatives come to the hospital for relevant examinations. The same gene mutation was found in her father. He was sixty-five years old with hypertrophic cardiomyopathy diagnosed by echocardiogram while her mother was healthy. He had the symptoms of chest tightness and shortness of breath. His ECG showed sinus rhythm with ST-T segment change. No myocardial fibrosis was found in his cardiac MRI (Figure3).

She has four siblings, only one of which had been diagnosed with hypertrophic cardiomyopathy by echocardiogram. He was thirty-four years old and in good condition before with no symptoms of hypertrophic cardiomyopathy. The same heterozygous mutation was found in TNNI3. ST-T segment change was found in his ECG and his cardiac MRI showed myocardial fibrosis (Figure 4).

Figure1. Case 1: The proband. (A) Sequencing analysis of exon 8 in TNNI3. (B) The representative image of ECG. (C) The representative image of echocardiography. (D) The representative image of MRI.
Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors’ institutional review board or equivalent committee.

Informed consent: Informed consent has been obtained from all individuals included in this study.
A novel TNNI3 gene mutation (c.235C>T/ p.Arg79Cys) found in a thirty-eight-year-old women...

3 Discussion

The MYH7, MYBPC3, TNNT2 and TNNI3 are the predominant genes causing HCM in Chinese population [4, 5]. In this case, we screened the four genes of the proband and her families and found a novel mutation in TNNI3. The present study is the first case with HCM who had a p. Arg79Cys mutation in TNNI3, which has never been reported before as a gene mutation responsible for HCM. The mutation of TNNI3 accounts for about 1-5% of patients with definitely genotyped HCM, but different phenotypes may be present [6]. It is estimated that mutation of TNNI3 is responsible for HCM. Most mutations in TNNI3 described up till now are found in exon 7 and 8, with some of these mutations found more frequently than others [7]. Concordantly, we also identified the mutation in exon 8.
In conclusion, we hypothesized that the Arg79Cys mutation in TNNI3 leads to a slow development of cardiac hypertrophy and the phenotype of this gene mutation is diverse.

Acknowledgment: Research project of Jiangsu Provincial Commission of Health and Family Planning (YG201501)

Conflict of interest: Authors state no conflict of interest.

References


