

A novel mutation of the *LMNA* gene in a family with dilated cardiomyopathy, conduction system disease, and sudden cardiac death of young females

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Abstract The *LMNA* gene, which encodes the nuclear envelope protein lamin A/C, is considered to be the most common autosomal disease gene associated with familial dilated cardiomyopathy. To date, each mutation of the *LMNA* gene has been associated with a specific disease phenotype. Clinical data, family histories, and blood samples were collected from 27 biological members of a family with dilated cardiomyopathy, prominently occurring as heart failure and conduction system disease with a high incidence of sudden cardiac death in young females. Twelve exons of the *LMNA* gene were screened for nucleotide alterations. A novel insertion mutation (nucleotide 1526insA, amino acid T510Y) in exon nine of the *LMNA* gene was identified in seven subjects (7/27, 25.9 %). This reveals that the *LMNA* gene insertion mutation (T510Y frameshift mutation) can cause dilated cardiomyopathy, conduction system disease, and sudden cardiac death without skeletal myopathy, clinically manifested with early onset, severe symptoms, and poor prognosis.

Keywords Family dilated cardiomyopathy · Genetics · Mutation · *LMNA*

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Introduction

Dilated cardiomyopathy (DCM) is a myocardial disorder characterized by dilation of the cardiac chambers and impaired systolic contraction, and is often associated with severe arrhythmias [1]. It is a major cause of congestive heart failure. Despite improvements in therapy, DCM is still a chief indication for heart transplantation worldwide. Virus infection, immune factors, and genetic defects are considered to be the main causes of DCM. However, the cellular and molecular bases are poorly understood. With the identification of genetic causes of DCM, it has become increasingly apparent that inherited, familial DCM (FDC) is more common than previously thought [2].

DCM is genetic in approximately 30 % of patients, and can be inherited in an autosomal dominant [3], X-linked [4, 5] autosomal recessive [6, 7], or mitochondrial [8, 9] manner. In more than 90 % of the cases, the mode of inheritance is autosomal dominant [10]. To date, at least 22 genes have been identified as associated with FDC, among which *LMNA* gene mutations are the most common.

LMNA gene mutations can result in diverse phenotypic expressions; at least eleven diseases are referred to as “laminopathies” [11], including Emery–Dreifuss muscular dystrophy (EDMD) [12], Dunnigan-type family partial lipodystrophy [13], Hutchinson–Gilford progeria syndrome [14], and DCM [15]. Recently, arrhythmogenic right ventricular cardiomyopathy patients without desmosomal gene mutations were also found to be associated with *LMNA* variants [16].

In this report, we describe a novel lamin A/C gene mutation in a large family with DCM. The disease is manifested in this family as heart failure, conduction system disease, and a high incidence of SCD in females at a young age, expanding the array of DCM phenotypes associated with lamin A/C gene mutations.