

Complex phenotype linked to a mutation in exon 11 of the lamin A/C gene: Hypertrophic cardiomyopathy, atrioventricular block, severe dyslipidemia and diabetes

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Abstract

The lamin A/C (LMNA) gene encodes lamins A and C, which have an important role in nuclear cohesion and chromatin organization. Mutations in this gene usually lead to the so-called laminopathies, the primary cardiac manifestations of which are dilated cardiomyopathy and intracardiac conduction defects. Some mutations, associated with lipodystrophy but not cardiomyopathy, have been linked to metabolic abnormalities such as diabetes and severe dyslipidemia. Herein we describe a new phenotype associated with a mutation in exon 11 of the LMNA gene: hypertrophic cardiomyopathy, atrioventricular block, severe dyslipidemia and diabetes.

A 64-year-old woman with hypertrophic cardiomyopathy and a point mutation in exon 11 of the LMNA gene (c.1718C>T, Ser573Leu) presented with severe symptomatic ventricular hypertrophy and left ventricular outflow tract obstruction. She underwent septal alcohol ablation, followed by Morrow myectomy. The patient was also diagnosed with severe dyslipidemia, diabetes and obesity, and fulfilled diagnostic criteria for metabolic syndrome. No other characteristics of LMNA mutation-related phenotypes were identified. The development of type III atrioventricular block with no apparent cause, and mildly depressed systolic function, prompted referral for cardiac resynchronization therapy.

In conclusion, the association between LMNA mutations and different phenotypes is complex and not fully understood, and can present with a broad spectrum of severity.

Keywords:

Hypertrophic cardiomyopathy; Lamin A/CLMNA gene; Dyslipidemia; Diabetes; Atrioventricular block