Spectrum of mutations in Hypertrophic Cardiomyopathy main genes among Tunisian patients

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Introduction

Hypertrophic Cardiomyopathy (HCM) is a common genetic cardiac disorder, caused by mutations in genes encoding for sarcomere proteins and transmitted in an autosomal dominant form. It is characterized by hypertrophy in the left ventricle, especially the septum. HCM is one of the most common causes of sudden cardiac death in the young with an estimated prevalence of 1 : 500 in the general population. However, The clinical profile and the genetic basis of HCM has not previously explored in Tunisia.

Aim of the study

The aim of this study is to determine the mutational spectrum of the main sarcomeric genes (MYH7, MYBPC3, TNNT2, TNNI3, ACTC1, TNNC1, MYL2, MYL3, TPM1) in a cohort of 45 HCM patients in Tunisia.

Table : **Main characteristics of HCM patients with sarcomeric mutations**

Patients ID	*Sex*	*Gene*	*Mutation*	*Onset age*	*Current age*	*Septum size*	*Family history HCM*	*Family history SCD*	*Symptoms*
N29	F	*MYH7*	c.2792A>C (p.E931A)	60	61	21	No	No	Chest pain, palpitation
N22	M	*MYH7*	c.5779A>T (p.I1927F)	36	37	15	No	No	Palpitation
N17	M	*MYH7*	c.3016G>A (p.A1006T)	74	74	17	No	No	Palpitation
N16	F	*MYH7*	c.4909G>A (A1637T)	72	76	18	No	Yes	Chest pain
N40	F	*MYH7*	c.2213G>A (p.S738 N)	56	D	20	No	Yes	Chest pain, dyspnea
N2	M	*MYBPC3*	c.530G>A (p.R177H)	56	58	15	No	No	Chest pain
N50	M	*MYBPC3*	c.772G>A (p.E258K)	49	51	15	Yes	No	Chest pain, palpitation
N4	F	*MYBPC3*	c.772G>A (p.E258K)	70	73	17	No	No	Chest pain, dyspnea
N39	M	*MYBPC3*+ *MYH7*	c.3296G>A (p.G1099E); c.353C>T (p.S118 L)	30	40	26	No	No	Chest pain, dyspnea
N3	F	*MYBPC3*+ *MYH7*	c.772G>A (p.E258K); c.5639G>A (p.R1880H)	28	30	25	Yes	Yes	Chest pain
N44	F	*MYL3*	c.170C>A (p.A57D)	45	50	28	No	Yes	Chest pain, dyspnea
N46	M	*TNNC1*	c.23C>T (p.A8 V)	53	62	21	Yes	No	Chest pain, dyspnea
N20	M	*FLNC*	c.4651G>A (p.A1551T)	31	36	15	No	No	Chest pain
N31	F	*FLNC*	c.2375G>T (S792I)	60	63	16	No	No	Palpitation
N49	M	*FLNC*	c.2375G>T (S792I)	48	52	16	No	No	Chest pain
N11	F	*FLNC*	c.5996G>A (p.R1999Q)	74	79	22	No	Yes	Chest pain
Mutation, mean values				52 Years	55 Years	20 mm	$n=3$	$n=5$	
No mutation, mean values				48 Years	67 Years	21 mm	$n=8$	$n=9$	

SCD, sudden cardiac death.

Conclusion

The mutational background of HCM in Tunisia is heterogeneous. Unlike other Mendelian disorders, there were no highly prevalent mutations that could explain most of the cases.

Patients and Methods

We performed semiconductor chip (Ion Torrent PGM) next generation sequencing of the nine main sarcomeric genes (*MYH7, MYBPC3, TNNT2, TNNI3, ACTC1, TNNC1, MYL2, MYL3, TPM1*) in 45 Tunisian HCM patients.

Results

We found sarcomere gene polymorphisms in 12 patients (27%), with MYBPC3 and MYH7 representing 83% (10/12) of the mutations. One patient was homozygous for a new MYL3 mutation and two were double MYBPC3+MYH7 mutation carriers..