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Familial cardiomyopathy in patients affected by acute myocarditis is strongly associated to DSP gene mutations

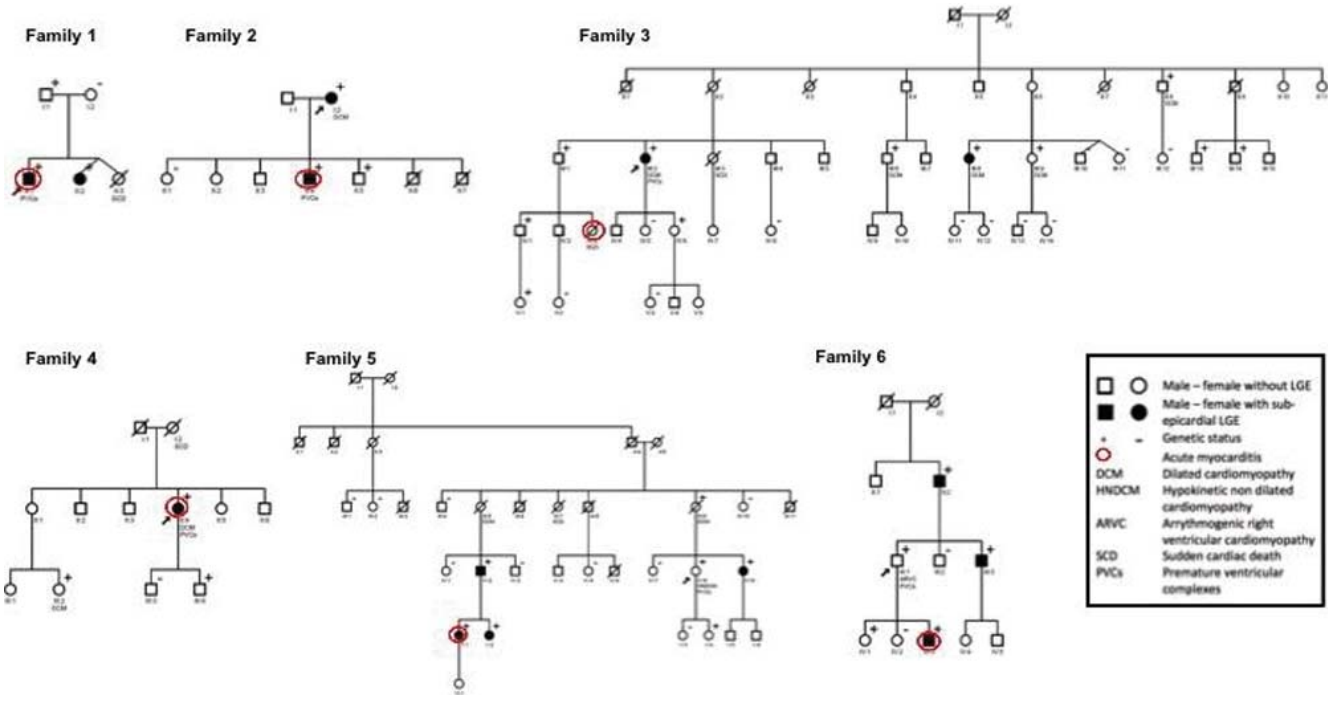
L. Marteau[1], F. Kyndt[2], C. Toquet[3], J.M. Serfaty[4], D. Guijarro[5], L. Le Gloan[1], G. Lande[1], J.B. Gourraud[1], K. Warin Fresse[4], E. Conan[1], A. Thollet[1], T. Le Tourneau[1], J.N. Trochu[1], V. Probst[1], N. Piriou[6]

[1]l'Institut du thorax, University Hospital of Nantes, Nantes, France; [2]University Hospital of Nantes, Molecular Genetics Department, Nantes, France; [3]University Hospital of Nantes, Pathology Department, Nantes, France; [4]University Hospital of Nantes, Cardiac and Vascular Radiology, Nantes, France; [5]Groupe Hospitalier Mutualiste, Institut Cardio-Vasculaire, Grenoble, France; [6]University Hospital of Nantes, Institut du thorax and Nuclear Medicine Department, Nantes, France

Background: The link between acute myocarditis (AM) and familial cardiomyopathy remains unclear.
Purpose: To assess the clinical significance of AM in families with cardiomyopathy.
Methods and results: We describe the pedigree of 6 families with at least one familial case of AM and a familial history of cardiomyopathy or sudden death (SD). AM was defined as an infarct-like clinical presentation with normal coronary arteries and myocardial inflammation (MI) documented by cardiac magnetic resonance (CMR), or as an autopsy proven AM. Detailed familial pedigrees are shown in the picture. In family 1 to 5, genetic testing was triggered by the association of a documented case of AM with an index case of cardiomyopathy or early SD. In this setting, all genetic testing revealed a mutation in the desmoplakin (DSP) gene. In family 1, patient II.1 (15 y.o) was diagnosed with AM, 6 months after his sister died suddenly at the age of 12. In family 2, patient II.4 (17 y.o) was diagnosed with AM. His mother had a DCM, with a CMR revealing the presence of MI. In family 3, patient IV.3 (22 y.o) died suddenly from an AM, attested by post-mortem autopsy. Her aunt had a DCM. In family 4, patient II.4 (41 y.o) had an AM, progressing toward a DCM. Her mother had died suddenly at the age of 39, and her niece had a DCM. In family 5, patient V.16 (9 y.o) presented 4 recurrent episodes of AM. Her cousin's mother had a DCM. In family 6, patient IV.3 had 3 episodes of AM, his father had previously been diagnosed with an arrythmogenic right ventricular cardiomyopathy (ARVC) with a desmoglein 2 (DSG2) mutation. Table shows detailed genotype-phenotype relationship in all mutation carriers screened in the 6 families.
Conclusion: AM is strongly associated to desmosomal mutations when a familial history of cardiomyopathy is present, particularly in DSP gene. In these families, DCM phenotype and SD are frequent, and a notable proportion of isolated LGE suggestive of myocardial fibrosis is present in asymptomatic relatives. These results highlight the need for a comprehensive familial screening in case of AM.

Phenotypes observed in mutation carriers

	Mutation	DCM	ARVC	AM	Isolated LGE (no cardiomyopathy, no AM)
Family 1 (n=3)	DSP	0	0	1	1
Family 2 (n=3)	DSP	1	0	1	0
Family 3 (n=11)	DSP	5	0	1	0
Family 4 (n=3)	DSP	2	0	1	0
Family 5 (n=7)	DSP	2	0	1	3
Family 6 (n=5)	DSG2	0	1	1	1



Family Pedigrees