# Familial idiopathic dilated cardiomyopathy

Pietro Vincenzo Fragola, M.D., Camillo Autore, M.D., Antonella Picelli, M.D., Luigi Sommariva, M.D., Dario Cannata, M.D., and Mario Sangiorgi, M.D.
*Rome, Italy*

The extent to which genetic factors may influence the pathogenesis of idiopathic dilated cardiomyopathy (IDC) remains a controversial issue. There have been occasional reports of an autosomal dominant pattern of inheritance in some families,[1-3] and an X-linked inheritance has also been suggested.[3a] Other investigators[4-8] have found a familial aggregation of IDC ranging from 2% to 50%. However, differences in methods of assessing data (family history, questionnaires, ECG) preclude direct comparisons of any conclusions concerning the incidence of familial IDC in these reports.

Forty-three patients with IDC were seen consecutively at our institution between January, 1985, and December, 1986. Twelve (probands: 11 male and one female, mean age 44 ± 12 years) consented to a familial screening. The diagnosis of IDC was based on echocardiographic evidence of an enlarged left ventricle (internal diastolic diameter >57 mm or exceeding the 95% prediction interval) with poor function in the absence of clinically significant coronary artery disease or any other cardiac or systemic disease that could produce myocardial damage; in the four probands aged ≥50 years and in a 23-year-old patient (who subsequently underwent transplantation), results of ventriculographic and coronary angiographic studies confirmed the diagnosis. None had a family history of dilated cardiomyopathy.

Forty-four first-degrees relatives of these 12 patients (four parents, 20 siblings, and 20 offspring) underwent clinical, echocardiographic, and ECG examinations. In seven siblings (one male and six females, mean age 56 ± 7 years) a diagnosis of IDC was made; in two of them the diagnosis was confirmed by coronary angiographic and ventriculographic studies. None of them had echocardiographic signs of right ventricular involvement (mean right ventricular end-diastolic diameter = 18 ± 2 mm). In another sibling, a 23-year-old boy with recurrent episodes of tachyarrhythmias, results of echocardiography showed

From the Department of Internal Medicine, II University of Rome.
Reprint requests: Pietro Vincenzo Fragola, M.D., Via A. Torlonia 12, 00161 Rome, Italy.

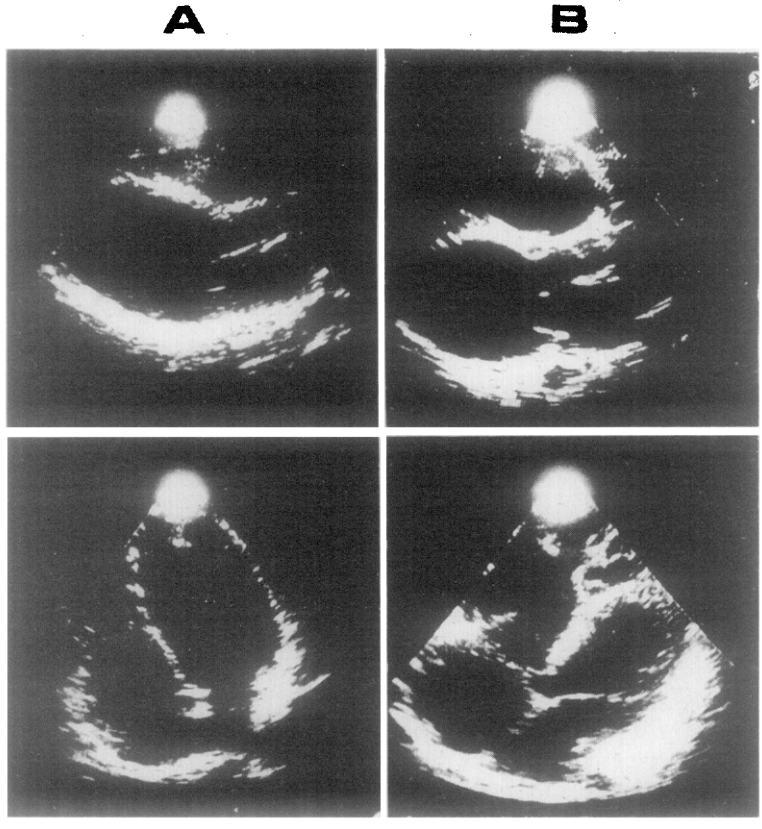


**Fig. 1.** Cross-sectional echocardiograms. *Top,* Long-axis view. *Bottom,* Apical four-chamber view. *A,* Nineteen-year-old boy with IDC (propositus). *B,* His 23-year-old brother with right ventricular dysplasia; note particular involvement of infundibulum and apex of right ventricle.

**Table I.** Family studies: Collected data from affected relatives and from relatives with uncertain diagnosis

| *Case No.* | *Age (yr)* | *Sex* | *Symptoms* | *ECG* | *LVDD (mm)* | *FS (%)* | *VCFm (circ/sec)* | *Diagnosis* |
|---|---|---|---|---|---|---|---|---|
| 1* | 63 | F | NYHA II | LVH | 58 | 21 | 0.81 | IDC |
| 2* | 66 | F | NYHA II | ST | 60 | 20 | 0.70 | IDC |
| 3* | 49 | F | None | LQRS | 53 | 23 | 0.81 | IDC |
| 4 | 23 | M | NYHA II | RAD, PVB, VT | 61 | — | — | RVD |
| 5** | 53 | M | None | LVH | 56 | 27 | 0.92 | IDC |
| 6*** | 60 | F | NYHA II | LVH, LAH | 63 | 24 | — | IDC |
| 7*** | 52 | F | NYHA II | LVH | 75 | 20 | — | IDC |
| 8*** | 50 | F | None | Normal | 55 | 27 | — | IDC |
| *Relatives with uncertain diagnosis* | | | | | | | | |
| 9**** | 54 | F | None | Normal | 49 | 27 | 0.96 | ? |
| 10**** | 47 | F | None | LBBB | 47 | 32 | 1.08 | ? |
| 11** | 57 | F | NYHA II | LVH | 51 | 33 | 1.13 | ? |

LVH = left ventricular hypertrophy; LAH = left anterior hemiblock; LBBB = left bundle branch block; ST = abnormalities of ventricular repolarization; LQRS = low-amplitude QRS complexes; RAD = right-axis deviation; PVB = premature ventricular beats; VT = ventricular tachycardia; LVDD = left ventricular diastolic diameter; FS = fractional shortening; VCFm = mean velocity of circumferential shortening; IDC = idiopathic dilated cardiomyopathy; RVD = right ventricular dysplasia; ? = uncertain diagnosis; NYHA = New York Heart Association.
*/**/***/****Members of the same family.

a severely enlarged and poorly contracting right ventricle (RV), paradoxical septal motion, and mild dilatation of the left ventricle (LV) with a RV/LV end-diastolic diameter ratio of 0.9; thus, right ventricular dysplasia (RVD) with left ventricular involvement was diagnosed[9] (Fig. 1). His brother (the proband) showed mild enlargement of the right ventricle at echocardiography (right ventricular end-diastolic diameter = 26 mm; RV/LV ratio = 0.40).

Among the affected relatives (seven with IDC and one with RVD; Table I), five were symptomatic (New York Heart Association class II); distinct ECG abnormalities were found in seven: a pattern of left ventricular hypertrophy in four, diffuse abnormalities of ventricular repolarization in one, low amplitude of QRS complexes in precordial leads in one, and right-axis deviation and frequent premature ventricular beats plus episodes of ventricular tachycardia that were of a left bundle branch block configuration in the patient with RVD. None had a history of recent viral infection or chronic alcohol abuse. In all affected females postpartum cardiomyopathy was excluded. Thirty-six relatives (mean age 29 ± 19 years) were judged unaffected by IDC, but two of them (both women, 54 and 57 years of age) had equivocal echocardiographic signs of myocardial involvement and one (a 47-year-old woman) had a left bundle branch block (Table I).

Familial dilated cardiomyopathy presumably is not as rare as previously believed, even though the role (causative or not) of genetic factors is still unclear. In our study the familial occurrence of IDC was 33% (4 of 12 families); a definite pattern of inheritance could not be assessed because in each family affected members were found in the same generation. This proportion of familial aggregation is similar to that reported by others who used only patients with proved disease to estimate familial IDC[5,8]; thus, inappropriate methods of family screening would probably account for the low incidence of familial IDC found in large studies.[6,7,10] Furthermore, clinical, ECG, and echocardiographic features of sporadic and familial cases were substantially indistinguishable so that in this study a peculiar form of familial IDC, as suggested,[1,3] was not identified. Moreover, a definite diagnosis is required in the three first-degree relatives with ECG or echocardiographic abnormalities that were actually of uncertain significance; it is noteworthy that left bundle branch block may exist many years before the clinical onset of IDC and in these instances results of myocardial biopsy showed marked pathologic changes.[11] Finally, the finding of a family with both IDC and RVD raises the question of whether RVD can be considered as a separate entity or whether, in some cases, it represents almost a right ventricular dilated cardiomyopathy[12]; the variable morphologic expression of the disease in a single family remains an issue for further investigation.

**REFERENCES**

1. Ross RS, Bulkley BH, Hutchins GM, et al. Idiopathic familial myocardiopathy in three generations: a clinical and pathological study. Am Heart J 1978;96:170.
2. Voss EG, Reddy CVR, Detrano R, Virmani R, Zabriskie JB, Fotino M. Familial dilated cardiomyopathy. Am J Cardiol 1984;54:456.
3. Graber HL, Unverferth DV, Baker PB, Ryan JM, Baba N, Wooley CF. Evolution of hereditary cardiac conduction and muscle disorder: a study involving a family with six generations affected. Circulation 1986;74:21.
3a. Berko BA, Swift M. X-linked dilated cardiomyopathy. N Engl J Med 1987;316:1186.
4. Ando M, Tkao A, Mori K, Sekiguchi M. The mode of inheritance in idiopathic cardiomyopathy: a preliminary report. In: Sekiguchi M, Olsen EGJ, eds. Cardiomyopathy. Baltimore: University Park Press, 1980:429.
5. Sekiguchi M, Hasegawa A, Ando M. A proposal for analyzing the familial occurrence of cardiomyopathy in the clinical situation. In: Sekiguchi M, Olsen EGJ, eds. Cardiomyopathy. Baltimore: University Park Press, 1980:445.
6. Fuster V, Gersh BJ, Giuliani ER, Tajik AJ, Brandenburg RO, Frye RL. The natural history of idiopathic dilated cardiomyopathy. Am J Cardiol 1981;47:525.

7. Bagger JP, Baandrup U, Rassmussen K, Møller M, Vesterlund T. Cardiomyopathy in Western Denmark. Br Heart J 1984;52:327.
8. Keren A, Billingham ME, Weintraub D, Stinson EB, Popp RL. Mildly dilated congestive cardiomyopathy. Circulation 1985;72:302.
9. Manyari DE, Duff HJ, Kostuk WJ, et al. Usefulness of noninvasive studies for diagnosis of right ventricular dysplasia. Am J Cardiol 1986;57:1147.
10. Michels VV, Driscoll DJ, Miller Jr FA. Familial aggregation of idiopathic dilated cardiomyopathy. Am J Cardiol 1985; 55:1222.
11. Kuhn H, Breithardt G, Knieriem HJ, et al. Prognosis and possible presymptomatic manifestations of congestive cardiomyopathy. Postgrad Med J 1978;54:451.
12. Fitchett DH, Sugre DD, MacArthur CG, Oakley CM. Right ventricular dilated cardiomyopathy. Br Heart J 1984;51:25.

## Ventricular tachycardia and sudden death in myotonic dystrophy

Shuichi Hiromasa, M.D., Takayuki Ikeda, M.D., Kouji Kubota, M.D., Nobu Hattori, M.D., Humberto Coto, M.D.,* Claudio Maldonado, M.S.,* and Joel Kupersmith, M.D.* *Ishikawa, Japan; and Louisville, Ky.*

Myotonic dystrophy is an autosomal dominant neuromuscular disease characterized by rigidity and degeneration of the skeletal muscle, cataract formation, gonadal atrophy, frontal baldness, and mental impairment. Cardiac involvement in this disease is well known. Since such cardiac lesions tend to involve the specialized conducting system, development of abnormal impulse formation and conduction is frequent.[1-3]

Previously, we reported[4] a family afflicted with myotonic dystrophy that showed diffuse cardiac conduction disturbances. One member of this family (case No. 1) with clinical features of muscular dystrophy was found to have multiple episodes of spontaneous sustained ventricular tachycardia (VT). This patient underwent exhaustive right and left ventricular mapping and electrophysiologic studies.[4] This VT was easily reproduced and terminated by right ventricular programmed electrical stimulation, suggesting a reentry mechanism. The resultant QRS configuration was similar to that seen during spontaneous attacks. Also, mapping performed in both ventricles suggested that this tachycardia arose from the right ventricle. Furthermore, His bundle ECG revealed HV interval prolongation. This finding indicated that the first-degree atrioventricular (AV) block observed on the patient's ECG resulted from depressed His-Purkinje conduction. An echocardiogram revealed mitral valve prolapse (MVP). However, during multiple physical examinations, no clicks or murmurs were detected during careful auscultation performed by several examiners, indicating that the echocardiographic diagnosis of MVP was clinically irrelevant. Usually, in patients with MVP and VT, this arrhythmia originates presumably as a result of increased tension of the papillary muscle secondary to the prolapsing valve, and not from the right ventricle, as is the case with our patient. Therefore, the association in this patient of VT and MVP is very unlikely. Other studies, including right and left heart catheterizations and endomyocardial biopsy, showed no evidence of cardiomyopathy; also an exercise stress test with thallium imaging failed to demonstrate perfusion abnormalities, ischemic ST-T changes, or exercise-induced ventricular arrhythmias.

Since our initial investigation,[4] we followed this patient for 30 months. Despite multiple pharmacologic interventions including lidocaine, quinidine, procainamide, disopyramide, mexiletine, diltiazem, and propranolol, he continued to have short runs of VT as well as episodes of spontaneous sustained VT, documented by serial ambulatory continuous ECG recordings (Fig. 1). This ambulatory continuous ECG recording also showed occasional episodes of possible atrial tachycardia at 120 to 130 bpm. While this finding might suggest the possibility of an underlying sick sinus syndrome, subsequent ECGs and Holter monitors obtained during the patient's long-term follow-up failed to demonstrate the presence of such condition. Serial standard ECGs did not show any significant changes suggesting progression of intracardiac con-

From the First Department of Internal Medicine, Kanazawa University School of Medicine; and *Cardiovascular Division, University of Louisville School of Medicine.

Reprint requests: Shuichi Hiromasa, M.D., Cardiovascular Division, University of Louisville, School of Medicine, 550 S. Jackson St., Louisville, KY 40202.

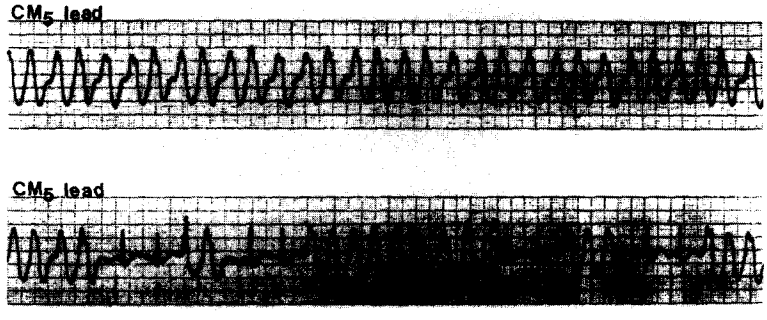


**Fig. 1.** Ambulatory continuous ECG recording obtained during follow-up and showing VT and a possible atrial tachycardia with an approximate atrial rate of 130 bpm.