

Familial right ventricular dilated cardiomyopathy

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SUMMARY Cardiomyopathy of unknown cause occurred in three of six siblings. The course of the illness was marked by life threatening supraventricular and ventricular arrhythmias, sinoatrial block, atrioventricular block, and embolism (in one patient). The disease was characterised by right ventricular dilatation. Two of the three patients died aged 32 and 48.

No new cases of the disease were found when a further 33 family members from three generations were investigated.

Dilated cardiomyopathy¹ is characterised by dilatation of the left or right ventricle or both and an increase in the weight of the heart. Patients with dilated cardiomyopathy may have atrial or ventricular arrhythmias and heart failure due to impaired systolic left and right ventricular function, and they often die at an early age. There are several published reports of the familial occurrence of dilated cardiomyopathy.²⁻⁵ In 1981, Fitchett *et al* described a type of dilated cardiomyopathy in which right ventricular involvement was most pronounced.⁶

We report three cases of dilated cardiomyopathy that occurred in a family of six siblings. Two died prematurely, one of them before our investigations were completed; necropsy was not performed. To elucidate a possible hereditary cause of the condition we investigated a further 33 family members in three generations.

Patients and methods

All eligible living family members underwent physical examination, radiography of the chest, and electrocardiography. The histories of those who had died were derived from case records or were supplied by the family. Initially we investigated only the parents, siblings, and children of siblings of the patients, but the study was extended to siblings of the mother because of reports of unidentified heart disease in three other members of her family. The father's sib-

lings and their families were not investigated because there was no evidence from the family to suggest other cases of heart disease among his relatives.

CASE 1

This woman was the third child in a family of six siblings. She was a moderate drinker and smoked about 10 cigarettes a day. She had experienced dyspnoea on exertion since the age of 26. Eight years later she was awarded a disability pension because of dyspnoea, and at the age of 37 she had heart disease classified as New York Heart Association functional class III.

Her heart had been dilated since the age of 29, and four years later she was given digitalis for intermittent atrial fibrillation. Before digitalisation the electrocardiogram showed flattened T waves in all leads, and this was a constant finding throughout her illness. At the age of 42, right sided heart decompensation was demonstrated for the first time, and quinidine was prescribed for ventricular extrasystoles.

Two years later she had ventricular tachycardia with subsequent cardiac arrest despite treatment with quinidine. Two days after drug treatment had been stopped there was still intermittent ventricular tachycardia and cardiac arrest alternating with third degree atrioventricular block, and for this reason a pacemaker (CPI-Minilith P) was implanted. Other findings are given in the Table.

At the ages of 33 and 44 the patient had transient pulmonary infiltrates of undetermined cause. She died in hospital at the age of 48 years after an episode of ventricular fibrillation. Shortly before death she had two episodes of right sided hemiparesis.

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Table Data on cases 1 and 2

	Case 1 (F)			Case 2 (M)
	29	34	47	31
Blood pressure (mm Hg)			125/80	110/70
Auscultation			Normal	Normal
Weight (kg)	60			73
Height (cm)	153			173
Cardiothoracic ratio (cm)	14/27		19/26	17.5/33
Echocardiography and angiocardiography			Dilated RV and RA, LV volume normal with good contractility	Dilated RV and RA, LV volume normal but decreased contractility
Normal				Normal
LV catheterisation				
RV catheterisation:				
Cardiac output (l/m ²)	Rest 3.6	Exercise 4.1		2.6
	8.4†	7.4*		4.9†
Pulmonary wedge pressure (mmHg)	Rest 15/10-12	Exercise 16/10-15		12
	24/14†	26/18*		12‡
Pulmonary arterial pressure (mmHg)	Rest 21/14-19	Exercise 29/14-22		26/11-17
	35/20†	34/21*		30/11-14‡

RV, right ventricle; RA, right atrium; LV, left ventricle.
 *25 W for 3 minutes; †50 W for 5 minutes; ‡100 W for 5 minutes.

PATHOLOGICAL FINDINGS

The heart was enlarged and globoid, weighing 490 g (0.8% of body weight). The right side was grossly dilated (Fig. a, b, c). The left atrium was also slightly dilated, but the left ventricular cavity size appeared to be normal. There were no congenital abnormalities.

The cusps were normal, but the tricuspid ostium was dilated (132 mm; mitral ostium 108 mm). The endocardium of the right ventricular cavity was patchily thickened by fibrosis; there were no parietal thrombi, either in this cavity or on the left side. The tip of the pacemaker electrode was encased in endocardial fibrotic tissue posteromedially at the base of the right ventricle. The myocardium was pale with slightly increased fibrosis on the cut surface. There were no signs of recent or old infarction, and the coronary arteries were normal without atherosclerosis.

There were old small infarcts in the left hemisphere of the brain, both kidneys, and the spleen, although no parietal thrombi or their sequelae were seen in the left ventricle. Apart from slight chronic congestion the lungs were normal and there was no evidence of thromboembolism.

Sections from the right ventricle showed hypertrophy with fibre attenuation, fibrosis of the replacement type, and fatty infiltration. There was some diffuse infiltration of lymphocytes in the right atrium caused by implantation of the pacemaker electrode. The myocardium of the left ventricle showed similar but less pronounced changes.

Only the atrioventricular area of the conduction system was available for investigation (the top of the right atrium had been cut off at initial necropsy). Slight nonspecific fibrosis was seen in the bundle of

His and in the left main fascicle. There were no granulomas or inflammatory cell infiltration.

CASE 2

This 36 year old man was a brother of case 1. He was the youngest of six siblings. He was a moderate drinker and he smoked 10 cigarettes a day.

He had completed his military service without difficulty at the age of 20. He had experienced dyspnoea on exertion since the age of 31 years, and because of cardiomyopathy he was awarded a disability pension when he was 34 years old. At that time he had heart disease classified as New York Heart Association functional class III.

Since the age of 31 he had been treated with digoxin because of atrial flutter. Before digoxin treatment the electrocardiogram showed atrial flutter with 3:1 block, incomplete right sided bundle branch block, and a negative T wave in V2-V5. During exercise testing the His bundle electrocardiogram showed that two out of three impulses were blocked at the atrioventricular junction, and during exercise at 50 W for five minutes he developed 2:1 block. With additional exercise of up to 100 W 1:1 block developed with a heart rate of 264 beats/minute. Because the heart rate did not fall after exercise had stopped DC cardioconversion was given. Atrial flutter recurred a few days later despite quinidine treatment. Further findings are given in the Table.

CASE 3

This patient was the brother of cases 1 and 2. He was the fourth of six siblings. He drank very little alcohol and smoked few cigarettes.

He had completed military service without

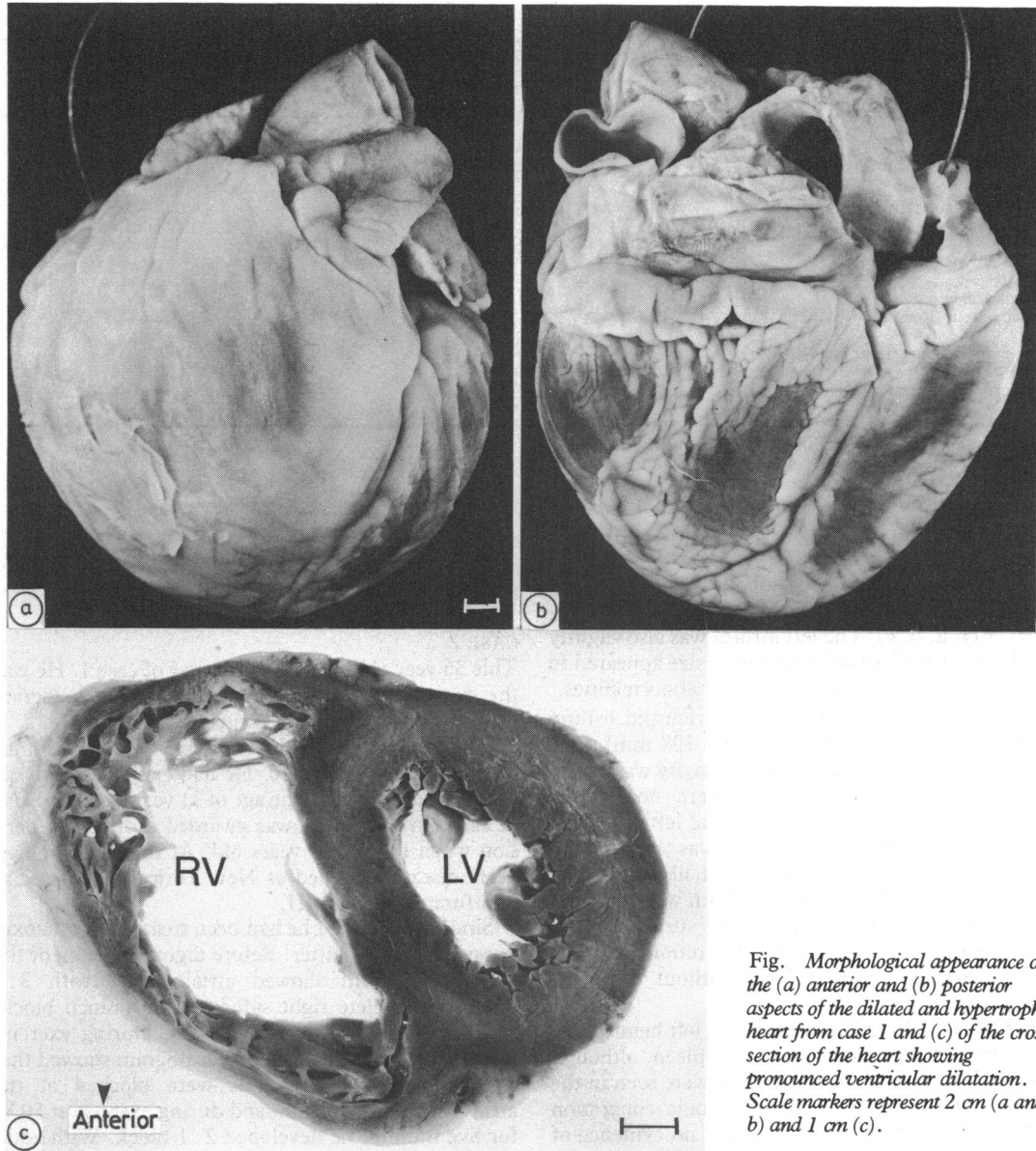


Fig. Morphological appearance of the (a) anterior and (b) posterior aspects of the dilated and hypertrophic heart from case 1 and (c) of the cross section of the heart showing pronounced ventricular dilatation. Scale markers represent 2 cm (a and b) and 1 cm (c).

difficulty. At the age of 24 he began to experience dyspnoea on exertion and stress induced palpitation. He was awarded a disability pension at the age of 30 because of heart disease (New York Heart Association functional class III).

During hospital admission at the age of 26 no decompensation of the heart was demonstrated. Cardiac auscultation was normal. Blood pressure was 120/80 mm Hg. Before medical treatment an electrocardiogram showed alternating sinus rhythm and

atrial flutter, with varying degrees of atrioventricular block; there were negative T waves in leads V2-V3. Radiography of the heart and lungs showed a cardiothoracic ratio of 0.59.

He was found dead in bed at the age of 32 years. Necropsy was not done.

OTHER FAMILY MEMBERS

Three other members of the family (all on the maternal side), who had died many years before our study,

were reported to have had heart disease. Data on them were incomplete and too unreliable for a diagnosis of cardiomyopathy. Three siblings, children of one of the patients' healthy siblings had electrocardiographic changes in V1. No other signs of cardiac disease were found in the 33 family members examined.

Discussion

There are other published reports of the occurrence of familial dilated cardiomyopathy.²⁻⁵ We believe that the three siblings we describe had the same cardiac disease, although the data in case 3 are limited because the patient died 16 years ago. No other cases of dilated cardiomyopathy have been found in the family.

Examinations carried out in cases 1 and 2 excluded diseases such as ischaemic, valvar, and congenital heart disease. Furthermore, it was not possible to demonstrate specific cardiac muscle disease or signs of pulmonary disease. A shared (unknown) environmental cause seems unlikely. The siblings did not live close to each other and there was an interval of 17 years between the appearance of the disease in the youngest patient (case 2) and manifestation in the oldest patient (case 1).

The symptoms, irregular palpitation of the heart and dyspnoea on exertion, started between the ages of 25 and 30 years. Two patients died at the ages of 32 and 48 years.

Although case 1 had had symptoms typical of left heart disease for many years, echocardiography and necropsy demonstrated mainly changes of the right side of the heart. Both right atrium and right ventricle were dilated, while the left atrium and ventricle were of normal size; similarly in patient 2 the right side of the heart was enlarged, although to a lesser degree.

Fitchett *et al* and Rowland *et al* described cases of dilated cardiomyopathy with predominantly right ventricular dilatation.⁶⁻⁸ The disease presented clinically as either right heart failure or arrhythmias and syncope. Our patients had arrhythmias, which were the cause of death in case 1 and probably also in case

3. In case 1 right heart failure was a late event. Unlike the patients investigated by Fitchett *et al* and Rowland *et al*, however, our patients had clinical signs of involvement of the left side of the heart. At necropsy there was gross and histological evidence for involvement of both sides of the heart in three of Fitchett's patients. We believe that our investigation adds further support to the concept of right ventricular dilated cardiomyopathy, which in our opinion represents one end of the spectrum of dilated cardiomyopathy rather than an independent type of (familial) cardiomyopathy.

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