Familial dilated cardiomyopathy- a case report from western Nepal

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ABSTRACT

Dilated cardiomyopathy (DCM) is a common cause of congestive cardiac failure all over the world. Most cases are idiopathic and sporadic. However, an increasing number are found to have a genetic basis which accounts for about 25.0-30.0% of cases all over the world. Different modes of inheritance and mutations have been implicated in these familial cases. Regardless of the type, they usually present in an advanced state with features of congestive cardiac failure or with complications like arrhythmia and sudden cardiac death and have a high mortality rate of 15.0-50.0% at 5 years. Hence in all DCM cases, detailed family history and if possible screening examination of the relatives is to be done so as to diagnose the familial cases in an early stage and prevent the likely complications. Here we present an interesting case of familial dilated cardiomyopathy (FDC) in which all four sons of the family are suffering from a heart disease while all the daughters are spared.

Keywords: Familial dilated cardiomyopathy, left ventricular ejection fraction, left ventricular end diastolic diameter, fractional shortening.

Dilated cardiomyopathy (DCM) constitutes 25.0% of all cases of congestive cardiac failure.[1] It is characterized by systolic dysfunction of the ventricles leading to dilatation of the ventricles and eventually failure. In most cases the cause is unknown; however it is considered to be an end result of myocardial insult of various etiologies. Today, an increasing number of cases are found to have a genetic basis which accounts for about 25.0-30.0% of cases all over the world[1]. Here we report an interesting case of familial DCM in a family from western Nepal.

CASE REPORT

A 54 year old male presented with acute onset breathlessness and vague chest pain. On examination he had blood pressure (BP) of 130/80mmHg, raised jugular venous pressure (JVP), crackles over the lung bases and a pansystolic murmur at the apex. A huge cardiomegaly with cardiothoracic ratio (CT ratio) of 0.733 was seen on chest X-ray (CXR). ECG revealed left axis deviation (LAD), left ventricular hypertrophy (LVH) and T wave inversion in I, avL, V4, 5, 6 leads. Echocardiography (Echo) showed a global hypokinesia with left ventricular ejection fraction (LVEF) – 30.0%, left ventricular end diastolic diameter (LVedd) -73.6mm, fractional shortening (fs) - 11.3% mild pulmonary arterial hypertension and moderate mitral regurgitation (MR). Cardiac enzymes were negative for ischemia. The patient was managed in the line of congestive cardiac failure (CCF) with frusemide, spironolactone, enalapril, carvedilol and digoxin. Aspirin was added to prevent thromboembolic complications. There was a dramatic improvement in the clinical symptoms within few months; Echo done 2 years later showed an increase in LVEF to 53.0% and to 62.0% in five years time when patient was 59 years of age and CT ratio in X-ray was decreased to 0.5.

His brother, a 70 year old male later presented with the similar complaints of vague chest pain and breathlessness. On examination he had B.P of 130/90 mm Hg, raised JVP, crackles over the lung bases and a systolic murmur at apex. Chest X-ray showed cardiomegaly with CT ratio=0.6; ECG-:LAD, LVH and T wave inversion in leads V5 and 6; echo- LVedd-62.7mm, fs- 16.0%, LVEF 32.0% with diastolic dysfunction, moderate MR, mild aortic regurgitation and moderate pulmonary arterial hypertension. He was also treated along similar lines. He showed improvement in symptoms soon and LVEF increased to 40.0% in 11 months time.

Both the brothers are non alcoholics; do not have history of any significant myocardial insult or any other associated medical problems. They had similar presentation and similar findings in echocardiography and ECG. Both have responded dramatically to conservative management. In their family they have two more brothers who are between the age of 60-70 years and who give a history of similar heart problem. Interestingly none of their three sisters have any health problem. They have children between the age of 30-40 years and none of them have developed any kind of

symptoms. Their father died at a young age due to unknown cause and mother died of heart failure in her sixties. Due to lack of proper documentation we cannot establish the pedigree confidently but the presence of idiopathic DCM in two members of the family suggest a diagnosis of familial DCM. The family members have been advised for a screening echocardiography and counseled about the risk associated. Genetic analysis could not be done.

DISCUSSION

Dilated Cardiomyopathy can be diagnosed based on the criteria given below (Manolio *et al*, modified):[2,3]

1. Ejection fraction of the left ventricle <0·45 (>2 SD) and/or fractional shortening <25.0% (>2 SD), as ascertained by echocardiography radionuclide scanning or angiography.
2. Left ventricular end-diastolic diameter >117.0% of the predicted value corrected for age and body surface area which corresponds to 2 SD of the predicted normal limit +5.0%.

Familial dilated cardiomyopathy is a condition where DCM is inherited due to various mutations in the genes encoding for the cytoskeletal and sarcomeric proteins in cardiac myocytes. According to the criteria in "Guidelines for the study of familial dilated cardiomyopathies" (Mestroni *et al*),[3] familial DCM can be diagnosed if:

1. Two or more affected relatives with DCM meet the above-mentioned criteria; or
2. a relative of a DCM patient has unexplained sudden death before the age of 35 years

And the clinical status of members of families with familial DCM can be defined according to the following criteria:[3]

Major criteria

· Defined criteria for dilated cardiomyopathy (as stated above).

Minor criteria

1. Unexplained supraventricular (atrial fibrillation or sustained arrhythmias) or ventricular arrhythmias, frequent(>1000 . 24 h"1) or repetitive (three or more beats with >120 beats . min"1) before the age of 50;
2. Left ventricular dilatation >112% of the predicted value
3. Left ventricular dysfunction: ejection fraction <50.0% or fractional shortening <28.0%;
4. Unexplained conduction disease: second or third degree atrioventricular conduction defects, left bundle branch block, sinus nodal dysfunction;
5. Unexplained sudden death or stroke before 50 years of age;
6. Segmental wall motion abnormalities in the absence of intraventricular conduction defect or ischemic heart disease.

Clinical status of the family members of the patient with DCM is considered to be:

· *Affected with familial DCM if:*

o presence of the major criteria (left ventricular dilatation and systolic dysfunction) or

o left ventricular dilatation (>117.0%) and one minor criterion or

o three minor criteria

· Unknown if : presence of one or two minor criteria

· Unaffected if : individuals with normal hearts or the presence of other causes of myocardial disease

Various conditions that damage the cardiac myocytes may lead to an end result resembling dilated cardiomyopathy. Hence the following conditions have to be ruled out before establishing the diagnosis as idiopathic or familial dilated cardiomyopathy[3].

1. blood pressure higher than 160/110 mmHg, documented and confirmed through repeated measurements;
2. obstruction (more than 50.0%) of a major branch of the coronary artery;
3. alcohol intake more than 100g/day;
4. persistent high rate supraventricular arrhythmia;
5. systemic diseases;
6. pericardial diseases;

Clinically patients with DCM may be asymptomatic or just have fatigue and palpitation for a long time. They may present in late stage with CCF, arrhythmias, thromboembolic complications or even with angina like chest pain. ECG may show sinus tachycardia, atrial fibrillation, ventricular arrhythmias, left atrial abnormality, low voltage diffuse nonspecific ST-T-wave abnormalities or intraventricular and/or AV conduction defects. . Cardiac arrhythmia as the presenting feature is specially noticed in cases of familial DCM with mutation in *laminA/C* gene. Since genetic testing and mutation screening is not yet available for routine use, familial DCM can be diagnosed only by taking a proper family history and screening of the family members with clinical examination, ECG and echocardiography. In a study[4] it was seen that the only clinical distinction of familial DCM from sporadic onset was its early onset and a greater ejection fraction in patients when diagnosed. The simultaneous presence of other

conditions as listed below also points to a familial DCM. Various mode of inheritance were recognized which are as follows:

- autosomal dominant, the most frequent form
- autosomal recessive , characterized by worse prognosis
- X-linked FDC , with different mutations of the dystrophin gene
- a novel form of autosomal dominant DCM with subclinical skeletal muscle disease
- FDC with conduction defects
- rare unclassifiable forms

Familial DCM is treated in the same manner as any case of DCM. General measures include patient education, salt and fluid restriction, treatment of hypertension, limitation of alcohol intake, control of body weight, and encouraging moderate exercise, preferably aerobic in a controlled environment. Therapeutic measures include diuretics including spironolactone, angiotensin converting enzyme inhibitors, cardioselective B blockers, antiplatelet agents and digoxin if required. Dramatic response is seen to conservative management. However complications like heart failure, arrhythmia, and thromboembolic episodes are common in such patients and if left untreated the 5 yr mortality ranges between 15.0-50.0%.[5]

Hence in any case of DCM, taking proper family history and screening of family members is very important for early diagnosis and prevent the complications and mortality associated with it.

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