Familial Dilated Cardiomyopathy and Human Leucocyte Antigen

A Report of Two Family Cases

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SUMMARY

Two familial cases of dilated cardiomyopathy were evaluated by HL-A typing. In the case of the first family, the mode of inheritance is likely to be an autosomal dominant trait. Only the affected individuals carried the identical HL-A haplotype (A2, Bw54, Cw1, DR4, DQw3), while the unaffected members do not share this pattern. In the second family case, the disease is probably inherited by autosomal recessive traits. All of the family members examined shared the identical HL-A haplotype (A24, Bw52, DR2, DQw1), but only the affected individuals were homozygous for this haplotype.

Additional Indexing Words:
Dilated cardiomyopathy  Familial occurrence  HL-A association

THE specific etiology of dilated cardiomyopathy (DCM) is obscure. It has been suggested that the pathogenesis of DCM may be heterogenous. Immunological mechanisms have recently been implicated in some patients with DCM. However, little is known about the HL-A system in DCM. In this report, we describe 2 family cases with DCM in an attempt to evaluate HL-A haplotypes with the pathogenesis of the syndrome.

Case Report

Family case 1: A 36-year-old man had been well until December 1983, when he experienced his first episode precordial discomfort and dyspnca on moderate effort. He visited a neighboring doctor and was diagnosed as having congestive heart failure. He was referred to our Institute for treat-
ment and further evaluation. There was neither a family nor a personal history of hypertension, diabetes mellitus or rheumatic heart disease. He did not drink alcoholic beverages. His grandfather died of heart failure of unknown etiology at the age of 54. His father also died of intractable congestive heart failure, diagnosed as chronic myocarditis in our hospital, at the age of 52. The physical examination on admission showed a heart rate of 90/min and a blood pressure of 108/64 mmHg. An S4 gallop and a mild systolic regurgitant murmur at the apex were audible. An electrocardiogram showed left ventricular hypertrophy, depression of the ST-T segment in the left precordial lead and multifocal ventricular premature beats. The chest X-ray film of the patient showed mild pulmonary congestion and cardiomegaly (CTR: 59%). The echocardiogram revealed marked left ventricle (LV) dilatation and decreased wall motion (LVDd: 87 mm, LVDs: 78 mm, 10.3%FS). At the time of cardiac catheterization, an increased LV end-diastolic pressure (16 mmHg), a decreased cardiac index (2.41 L/min/m²), a marked LV dilatation, diffuse poor LV contraction and intact coronary arteries were documented.

Because a familial occurrence of DCM was suspected, his siblings were examined for evidence of cardiac disease. A 43-year-old brother, who is asymptomatic except for palpitation, had an abnormal electrocardiogram. The chest X-ray film of this brother showed no cardiomegaly (CTR: 43%), but his echocardiograms revealed LV dilatation and decreased LV wall motion (LVDd: 65 mm, LVDs: 52 mm, 20%FS). The intracardiac pressures and the cardiac index were within the normal range. Coronary arteriograms revealed no stenotic lesions. Thus, he was diagnosed as being a subclinical stage of DCM. Other family members did not show evidence of cardiac disease on electrocardiograms or echocardiograms. The pedigree and HL-A typing of the family 1 is shown in Fig. 1. The HL-A typing of the father was reconstructed from the data of other members.

![Fig. 1. The family pedigree and HL-A typing of the family of case 1.](image-url)
Family case 2: The patient is a 51-year-old female whose chief complaint is palpitation on mild effort. There is no family history of cardiac disease or consanguineous marriage. A Holter electrocardiogram revealed multifocal ventricular premature beats and non-sustained ventricular tachycardia. The physical examination was within normal limits, but the chest X-ray films showed mild cardiomegaly (CTR: 51%). The echocardiograms revealed mild LV dilatation and decreased LV wall motion (LVDd: 58 mm, LVDs: 46 mm, 21%FS). Since no causative cardiotoxic factors were found, she was diagnosed as a case of DCM. Her 49-year-old sister, who also complained of palpitation and mild dyspnea on effort, consulted our Institute. Her physical examination was within normal limits, except for an arrhythmia. The chest X-ray film showed no cardiomegaly (CTR: 49%). Multifocal ventricular premature beats and ST-segment depression in the left precordial leads were found on the electrocardiogram. LV dilatation and decreased LV wall motion were detected on the echocardiogram (LVDd: 57 mm, LVDs: 45 mm, 21%FS). She was also diagnosed as a case of DCM. The family pedigree and HL-A typing of the family members are shown in Fig. 2.

**DISCUSSION**

Hypertrophic cardiomyopathy (HCM), especially the hypertrophic obstructive form, frequently has a familial incidence and it is thought to be an autosomal dominant trait.\(^3,5\) By contrast, DCM is usually sporadic in incidence, and the familial form of DCM is rather exceptional. For example, Michels et al\(^4\) reported 168 cases of DCM, claiming that only 10 cases (6%) were familial. Because the familial form of DCM usually occurs in siblings and consanguineous marriages, it is thought to be an autosomal recessive
Recent reports have suggested that HCM shows clinical features similar to DCM during the course of the disease and that both HCM and cardiac disease with DCM-like clinical features may occur in members of the same family. In the 2 family cases described, the affected individuals showed no clinical features of HCM and there were no demonstrable HCM cases among the family members. Therefore, these cases appear to have familial DCM. For the first case, the pattern of familial occurrence was suggested to be the autosomal dominant mode of inheritance since the three generations were highly suspected to be involved. Such a case is thought to be a very rare form of familial DCM. In this case, the affected individuals shared the identical HL-A haplotype (A2, Bw54, Cw1, DR4, DQw3); unaffected individuals do not carry this pattern of HL-A haplotype. For the second case, all of the family members have the identical HL-A haplotype (A24, Bw52, DR2, DQw1), but only the affected individuals carry the homozygote of this haplotype. These data suggest that DCM is an autosomal recessive trait. It is well known that the HL-A genes are located in the region of the sixth chromosome that is supposed to control certain immune mechanisms. If the occurrence of DCM is influenced by the function of immunoresponsive or immunosuppressive genes related to the specific HL-A, there should be a significant correlation between the incidence of DCM and specific HL-A haplotypes. However, Yamaguchi et al reported that there is no correlation between the incidence of DCM and the specific HL-A (A, B). On the other hand there is a report that affected individuals shared the identical HL-A haplotype (A, B) in HCM with familial occurrence.

In these present familial cases, as has been mentioned in the reference, any specific antigens, that are speculated to correlate with the pathogenesis of DCM, cannot be identified. But all the affected individuals shared the identical HL-A typing, and the unaffected individuals did not carry such ones. Therefore this study suggests that an evaluation of HL-A typing in family members with familial DCM may be meaningful to detect or predict the affected persons.

REFERENCES


