Idiopathic Cardiomyopathy in Children

By Daniel K. Bloomfield, M.D., and Jerome Liebman, M.D.

This report describes a group of children, ages 3 to 13, who present unusual cardiac findings suggestive of the earliest stages of idiopathic cardiomyopathy. Idiopathic cardiomyopathy refers to an enlargement of the heart without apparent cause, but primarily due to muscular hypertrophy. The process is dominant in the left ventricle, but can involve other chambers, either primarily or secondarily after left ventricular failure. When hypertrophy involves the interventricular septum, there may be obstruction to left ventricular outflow and aggravation of the myopathic state. In the cases to be described, the diagnosis has been made largely on clinical grounds. The most important criteria are an abnormal left ventricular impulse with cardiomegaly, an abnormal jugular venous pulse, and an acquired characteristic murmur. Since most of the patients are asymptomatic and all are living, no autopsy or biopsy studies are presented. In the past, reports have been concerned with the late stages of cardiomyopathies. The majority of patients were adults who presented with congestive failure, and documentation was frequently made by autopsy. It is clear that little is known of the early natural history of the cardiomyopathy disease complex. It is our speculation that the cardiomyopathies run a protracted course measured best in decades rather than years. This study deals with what may be early manifestations of that process.

Methods

Twenty-seven cases have been identified during a 2-year period. All were studied because of a heart murmur. The patients were selected from the general outpatient clinic population of Babies and Childrens Hospital (17), were referred from outside our clinic population to the “Congenital Heart Clinic” at the hospital (8), or were private referrals (2). Seventeen of the 27 patients have been observed as general pediatric patients since infancy. Except for the private cases, each patient was given a complete history and physical examination by the resident staff before being examined by one or both authors. In each case, a diagnosis was made solely upon clinical evidence before electrocardiographic and x-ray studies, which are routine in our clinic, were done. Excluded were patients with a history suggestive of acute rheumatic fever and patients presenting with or having a history of congestive heart failure. These were excluded even though some may have represented varieties of cardiomyopathy in order to avoid any form of acute myocarditis.

Clinical Observations

Physical Findings

The clinical signs found are as follows:

1. An abnormal pattern in the venous pulsations of the neck (25/27, 93 per cent). When the children are placed supine with the head raised on a firm pillow so that venous pulsations can be seen at least halfway to the angle of the jaw, the X and Y descents stand out as prominent negative movements (fig. 1). A small A wave can often be seen rising from a plateau preceding the X descent, but the V wave appears as simply an abbreviated rise before another sharp Y descent. The movements are similar to those observed in constrictive pericarditis except that they occur in the presence of a normal venous pressure. In summary, the venous pulse appears as a plateau with two sharp dips. While the X and Y descents are occasionally dominant in normal children when viewed as described, the movements are never so sharp or so deep as those seen in the syndrome we are describing.

2. An abnormal, accentuated, left ventricular impulse (25/27, 93 per cent). The heart is invariably clinically enlarged by physical examination and all but two of the 25 showed
left ventricular hypertrophy by electrocardiogram or x-ray, although not necessarily both. The impulse can be described as a mild left ventricular rock (a term used by the late Dr. Paul Wood). This implies palpation of a systolic heave in the region of, or just lateral to, the cardiac apex occurring simultaneously with a retraction in the region of the right ventricle, a few centimeters to the left of the sternum in the fourth intercostal space. This counterclockwise movement (as viewed from below) can be seen as well as it can be felt.

3. A characteristic systolic ejection murmur (27/27, 100 per cent) (fig. 2). The murmur is best heard in the left parasternal region at the level of the third or fourth intercostal space, is of grade II-III/VI intensity, and is maximal at the end of expiration. It is usually transmitted well to the apex and the upper left sternal border. Less commonly, it can be heard well at the upper right sternal border. While it is frequently vibratory, more often it has the harsh diamond-shape quality of the ejection murmur associated with hypertrophic aortic outflow tract obstruction. In four patients thought clinically to have a systolic pressure gradient within the left ventricular outflow tract, the murmur was well transmitted into the neck. It was never heard maximally at the upper right sternal border. Since many of the patients have been observed by our clinics since birth, we have been able to document that the murmur has been acquired in each of the 16 cases in which evidence is available, i.e., the murmur was not heard by pediatricians during the routine pediatric care of the first few years of life.

4. A prominent third sound (10/27, 37 per cent). A third sound was heard in all 27 patients, as it is in most normal children, but was considered abnormally loud in only 10. The second sound was physiologically split in all instances.

All patients have been symptom free, except for five having ill-defined chest pain and two with mild fatigue associated with progressive cardiac enlargement during the period of observation.

Age, Race, Sex

The age distribution at the time of diagnosis is presented in table 1. The majority of cases were in the second half of the first decade. The age distribution of our clinic population is similar to that at any large pediatric hospital and has its full share of children under the age of 5. We have not observed any cases under the age of 3. The large majority of our cases have been in Negro chi-

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<td><strong>Age Distribution of Idiopathic Cardiomyopathy in Children</strong></td>
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Electrocardiograms from four children with early cardiomyopathies: (a) H.R., an 8-year-old Negro boy. This tracing shows increased voltages in limb leads. The deep Q waves in leads II, III, and aVF suggest septal hypertrophy. This is same patient whose withdrawal pressure tracings are shown in figure 8. (b) S.J., an 8-year-old Negro girl. This tracing shows increased voltages in precordial leads. (c) C.R., a 6-year-old Negro girl. The tracing shows increased voltage in aVF.

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Possibly of more significance is that 18 of 27 (67 per cent) have been male. In one family, two brothers appeared with signs of this cardiomyopathy, but no other familial pattern is evident to date.

Electrocardiogram

Electrocardiograms indicated left ventricular hypertrophy in 18 of 27 cases (67 per cent). All 18 showed increased QRS voltages in one or more leads that were beyond the limits of normal established by the criteria of Alimurung et al. The diagnosis of left ventricular hypertrophy by voltage changes alone was made in 10 cases. These abnormal voltages were observed in limb leads (fig. 3a) and precordial leads (fig. 3b). Three cases had ST-segment depression with flattening of T waves as well as QRS-voltage changes, suggesting a more advanced degree of hypertrophy (fig. 3c). Five of the 18 cases also showed tall peaking of the T waves (fig. 3d), a sign often seen in early left ventricular hypertrophy.

Other criteria standardized for age and heart rate were generally within normal limits. In a single case, the P-R interval was 0.02 second above normal. Duration of QRS was between 0.05 and 0.09 second in all except two patients, with minimal widening to 0.10 and 0.11 second. The Q-T interval was prolonged in a single case, a 13-year-old Negro girl with more advanced disease. Mean QRS axis was +54° (range -10 to +90°); mean T axis was +42° (range 0 to +55°). In only one case was the QRS-T axis gradient considered abnormal (60°). Derived frontal
plane vector loops were clockwise in 17 cases (all with QRS axis +50° or greater) and counterclockwise in 10 cases (all with QRS axis +45° or less). No arrhythmias were observed.

X-ray

The cardiac silhouette was abnormal in 23 of 27 cases (85 per cent). The abnormality has usually been limited to enlargement of the left ventricle evaluated in the postero-anterior and left anterior oblique views (fig. 4). In some instances, gradual progression has occurred (fig. 5) with the appearance of mild symptoms in two cases. In two of the four cases with normal x-rays, the electrocardiogram showed left ventricular hypertrophy. In the remaining two cases with normal x-rays, the cardiac impulse was characteristically abnormal and enlarged to the left.

Cardiac Catheterization

Right and retrograde left cardiac catheterizations were done in eight cases. Indications for catheterization have been the presence of chest pain, the clinical impression of a gradient in the left ventricular outflow tract, or in two cases, prominent hilar vessels, which suggested a left-to-right shunt that could have been due to anomalous origin of the left coronary artery. While the diagnosis of cardiomyopathy was likely in each case, it was considered essential to rule out conditions that were possibly amenable to surgical correction. Catheterization confirmed the characteristic venous pulses of the neck in six of eight cases (figs. 1, 6, and 7). In a single instance, in which the catheter was passed through the mitral valve into the left atrium, the left atrial tracing showed the characteristically sharp X and Y descents (fig. 7). Ventricular pressure curves were within normal contour limits, although a sharp early diastolic descent and a following plateau could be discerned (fig. 6). These tracings are reminiscent of pressure curves often seen in constrictive pericardial and endomyocardial disease except that the end-diastolic pressure is normal. In one case, a 20-mm. Hg gradient was demonstrated across the left ventricular outflow tract (fig. 8). Cardiac movements were entirely normal. The limited movements seen in subendocardial fibroelastosisb, 10 were not observed. Pressures were normal in all patients.

Discussion

This report describes essentially well children. Symptoms have been very few and, particularly with respect to the chest pain, difficult to define on a cardiac basis. Objective abnormal signs on physical examination, electrocardiogram, and x-ray have been demonstrated on repeated examinations. We propose that these abnormal findings in a group of otherwise healthy youngsters describe a syndrome. The prognosis for this syndrome is entirely unknown. Two cases have shown progression of the disease, but the others have remained stable. None has improved in the maximum of 2 years we have observed them.

It may be that many of these children will lose these findings during a period of matu-
Cardiac catheterization tracings from A. W., a 6-year-old Negro boy. Sharp X and Y descents dominate the right atrial tracing (RA). The right (RV) and left (LV) ventricular tracings are within normal limits although sharp diastolic dips and plateaus can be seen. Pressures are noted in mm. Hg.

Figure 6

Cardiac catheterization tracings from A. W., a 6-year-old Negro boy. Sharp X and Y descents dominate the right atrial tracing (RA). The right (RV) and left (LV) ventricular tracings are within normal limits although sharp diastolic dips and plateaus can be seen. Pressures are noted in mm. Hg.

Figure 7

Left atrial tracing in C.R., a 6-year-old Negro girl, showing typical sharp X and Y descents. Pressures are noted in mm. Hg.

ration. Then the syndrome might well be called a benign cardiac hypertrophy of childhood. There are studies, such as the one by Paulin and Mannheimer covering 108 normal children with physiologic murmurs and more recently by Marienfeld et al., who observed a benign course in 96 children 20 years after innocent murmurs were observed, which properly caution against undue stress being laid upon left parasternal murmurs. No other abnormal findings were described in their children, however, and this clearly separates the syndrome we are describing from the group with innocent murmurs. In addition, a long-term follow-up of patients with more classical ejection murmurs at the lower left sternal border or apex has not been noted.

As we have noted previously, the point that most interests us is that these children may represent the earliest stages of the unexplained cardiomyopathies that show congestive heart failure in adult life. When Spodick and Littman reviewed 72 cases of idiopathic myocardial hypertrophy, 93 per cent of the cases had no symptoms before age 20. The median survival following onset of symptoms was less than 18 months, but there

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are no clues as to when the myocardial process began. It is possible that we will find only a small fraction progress in that fashion, whereas the majority remain stable or progress so little that no symptoms occur. They could indeed be completely overlooked and pass as normal. This would be a situation not unlike that found in the history of histoplasmosis, which was first indicted as a uniformly fatal infection before skin testing clearly demonstrated the wide prevalence of past infection and its essentially benign nature. What is lacking in our cases of cardiomypathy is a specific diagnostic test that will clearly delineate this syndrome.

We have not attempted to make any classification among individual cases. Those that appear to represent early forms of hypertrophic outflow tract obstruction, first described by Sir Russell Brock and since observed with increasing frequency by several other investigators, may represent one pathway of progression. Simple idiopathic myocardial hypertrophy with eventual cardiac failure may represent another. Braunwald et al. have come to this conclusion from a different direction, having observed similar left ventricular angiograms in three adult patients, one with and two without hypertrophic subaortic stenosis. They speculated, as we do, that the same basic disease process may be responsible for a variety of clinical and hemodynamic pictures. Information on the role of chest pain is too fragmentary at this time to discern its importance in prognosis or classification.

We believe the high incidence of Negroes only reflects the character of our clinics and statistical analysis of this aspect has been deferred. The predominance of males, on the other hand, is clear. This finding is in keeping with the above-mentioned review of idiopathic cardiac hypertrophy where 81 per cent of cases were male.

The relationship of the jugular venous pulse to the syndrome may afford a clue to the basic physiology of the involved hearts. The sharp X and Y descents suggest abnormally rapid atrial and ventricular diastolic relaxation with the creation of accentuated negative pressures in the venous system. The myopathic state, which is symptomatically manifested primarily in the left ventricle, could be a disease of the entire myocardium, so that the events that register on a system as delicate as the venous pulse would be observed on the right as well as the left side of the heart. Braunwald et al. for example, described a family in which one member was found to have obstruction primarily to right ventricular outflow, while his two brothers showed left ventricular involvement, and suggested that both were different manifestations of the same basic disease. Since Dock and more recently Nixon have plausibly shown the third sound to be due to a sudden tensing of the mitral valve cusps and chordae, the rapid ventricular relaxation coupled with a more rigid diastolic elastic limit might also explain the accentuated third sound heard in more than one third of our patients.

The long-term follow-up of these patients will be directed toward the natural history and basic etiology of the condition. The latter part of the natural history of the progressive form of the disease is already well defined. Etiology, single or plural, remains a thorny problem. Since cardiomyopathies have been classified as independent events, or associated with many systemic diseases including connective tissue disease, amyloid,
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cirrhosis, nutritional deficiency, hypersensitivities, infections, alcoholism, and neuromuscular disease, there is much to be learned about why the myocardium is so affected. Contrariwise, it is entirely possible that in some instances the myocardium is already predisposed and vulnerable to the altered metabolism brought about in the above states. As a simple example, it has remained an enigma why when two patients, superficially indistinguishable, carry equal elevations of blood pressure for like periods of time, one falters in cardiac failure and the other lives on in good health. We are accustomed to explain that the one heart fails due to the excessive work load over a period of years, but this does not help explain why the other heart resists failure. It is entirely possible that a fundamental biologic difference exists between the two myocardia. An exaggeration of that same biologic difference could then explain the gradual appearance and progression of cardiac hypertrophy in the absence of hypertension. Our experience of finding these 27 cases over the brief span of 2 years leads us to believe that when this clinical picture is appreciated widely, far more insight will be gained into the problems posed by cardiomyopathies.

Summary

This report describes 27 cases of a clinical cardiomyopathic syndrome in clinically well children. Physical findings regularly observed include an abnormal left ventricular impulse, a prominent X and Y descent in the jugular venous pulse, and a characteristic, acquired, systolic murmur. These are associated with the laboratory findings of an enlarged left ventricle by electrocardiogram and x-ray. This syndrome may be the earliest manifestation of cardiomyopathic states, such as idiopathic myocardial hypertrophy or hypertrophic outflow tract obstruction, which usually appear in the third decade of life and beyond. The frequency of cases found suggests that the latter diseases, which are relatively rare, are possibly only the more malignant representatives of a broad spectrum of cardiomyopathic states.

References

On Science and Culture

In traditional societies, the great function of culture is to keep things rather stable, quiet, and unchanging. It has been the function of tradition to assimilate one epoch to another, one episode to another, even one year to another. It has been the function of culture to bring out meaning, by pointing to the constant or recurrent traits of human life, which in easier days one talked about as the eternal verities.

In the most primitive societies, if one believes the anthropologists, the principal function of ritual, religion, of culture is, in fact, almost to stop change. It is to provide for the social organism what life provides in such a magic way for living organisms, a kind of homeostasis, an ability to remain intact, to respond only very little to the obvious convulsions and alterations in the world around.

To-day, culture and tradition have assumed a very different intellectual and social purpose. The principal function of the most vital and living traditions to-day is precisely to provide the instruments of rapid change. There are many things which go together to bring about this alteration in man's life; but probably the decisive one is science itself. I will use that word as broadly as I know, meaning the natural sciences, meaning the historical sciences, meaning all those matters on which men can converse objectively with each other. . . . When we talk about science to-day, we are likely to think of the biologist with his microscope or the physicist with his cyclotron; but almost certainly a great deal that is not now the subject of successful study will later come to be. I think we probably to-day have under cultivation only a small part of the terrain which will be natural for the sciences a century from now. I think of the enormously rapid growth in many parts of biology, and of the fact, ominous but not without hope, that man is a part of nature and very open to study.

The reason for this great change from a slowly moving, almost static world, to the world we live in, is the cumulative character, the firmness, the givenness of what has been learned about nature. . . . Thus everything that is found out is added to what was known before, enriches it, and does not have to be done over again. This essentially cumulative irreversible character of learning things is the hallmark of science.—J. Robert Oppenheimer. "On Science and Culture." Encounter, October, 1962, p. 3.
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