The Diagnosis of Primary Endocardial Fibroelastosis

By Frank J. Sellers, M.D., John D. Keith, M.D., and James A. Manning, M.D.

The term endocardial fibroelastosis was first used by Weinberg and Himelfarb\(^1\) to describe the condition of infantile cardiomegaly in which the pathologic lesion consisted of varying degrees of fibroelastotic proliferation within the endocardium. It is now well recognized that there are two forms of endocardial fibroelastosis. The first is associated with numerous congenital heart defects and appears to be secondary to them or has occurred simultaneously during their development. The second is comprised of a group with a marked degree of endocardial thickening with no obvious explanation for it. The pathologic picture is sufficiently characteristic that pediatric pathologists in recent years have recognized it as a distinct entity and referred to it as primary endocardial fibroelastosis.\(^2\)

Vlad et al.\(^3\) published the electrocardiographic findings in 23 postmortem cases of primary endocardial fibroelastosis, and demonstrated a high incidence of left ventricular loading patterns. They did not distinguish between cases with and without valvular involvement. While no attempt was made to define clearly the diagnostic features of this group clinically, the electrocardiographic pattern was sufficiently suggestive to encourage us to assess the problem from this point of view.

The purpose of this paper, therefore, is to analyze the clinical, electrocardiographic or radiologic, and pathologic findings in a group of cases of primary endocardial fibroelastosis so that the clinical entity can be more accurately identified. Furthermore, we wish to compare the clinical and laboratory features of primary endocardial fibroelastosis with other similar conditions.

Case Material and Criteria for Diagnosis

The details of 25 autopsied cases of primary endocardial fibroelastosis and 33 cases with similar clinical findings were reviewed. These infants were seen between the years 1952 and 1960 at the Hospital for Sick Children, Toronto, and the Strong Memorial Hospital, Rochester, New York. The two groups may be defined as follows: group I, 25 cases proved at autopsy without valvular disease and with at least one electrocardiographic tracing in each case; group II, 33 cases diagnosed clinically that satisfied the criteria set out below and were observed 2 to 8 years from the onset of the illness.

The data collected from group-I cases were reviewed in detail. It was noted that the diagnosis had been made clinically during life in the cases with certain features. A reassessment of this material provided the criteria that were applied to the clinical group II. The criteria established were onset of congestive heart failure under 2 years of age; absence of organic heart murmurs; electrocardiographic evidence of left ventricular overloading; and abnormal T waves in leads V5 and V6.

Congestive heart failure was considered to be an essential feature of the clinical diagnosis of endocardial fibroelastosis. All cases proved at autopsy in our series had symptoms and signs of congestive heart failure before 21 months of life.

The absence of organic heart murmurs was a necessary criterion for the diagnosis of primary endocardial fibroelastosis in order to avoid the question of valvular abnormality. In no cases of endocardial fibroelastosis proved at autopsy in which the aortic, mitral, pulmonary, or tricuspid valves were normal was an organic heart murmur heard.

The electrocardiographic pattern associated with left ventricular overload appeared in 85 per cent of the autopsied cases and was present in a very similar percentage (78 per cent) in the group of 23 autopsied cases reported by Vlad et al.\(^3\) Therefore, this electrocardiographic pattern was included in the criteria for diagnosis. Similarly, flattening or inversion of the T waves in leads V5 and V6 occurred in 92 per cent of all postmortem cases. When flattening or inversion of the T wave occurred in lead V5, it was also present in lead V6.

If any of the following criteria (1 to 4) were

---

From the Department of Pediatrics of the University of Toronto, The Research Institute of the Hospital for Sick Children, Toronto, Canada, and the Department of Pediatrics, University of Rochester, Rochester, New York.

Aided by a grant from the Ontario Heart Foundation.

Circulation, Volume XXIX, January 1964
satisfied, left ventricular loading was considered to be present: (1) voltage of \( S \) in V1 of more than 20 mm.; (2) voltage of R in V6 of more than 20 mm.; (3) Q wave of more than 3 mm. in V5 and V6; (4) R/S ratio of V1 less than 0.8 mm. under 12 months of age and 0.2 mm. between 13 and 24 months of age; and (5) secondary flattening or inversion of the T wave in V5 or V6.

It will be seen from figures 1 to 3 that criteria 1, 2, and 3 are more definite than criterion 4. Criterion 5 was not always present in the autopsy-proved group but was considered necessary for the diagnosis on clinical grounds alone.

All the patients were treated with digitalis. Those treated early in the illness survived longer. They were then kept on digitalis for at least 2 years (fig. 4).

**Signs and Symptoms**

Dyspnea and tachycardia occurred in all cases in both groups. In cases with severe congestive heart failure grunting respirations and cyanosis were frequent. Rales in the chest were heard only occasionally. Congestive heart failure was made one of the criteria for diagnosis and thus was present in all cases in both groups. Gallop rhythm was most frequent in the cases with continued congestive heart failure.

**Figure 1**

Electrocardiogram in 3-month-old infant shows deep \( S \) in V1, tall R, Q, and deeply inverted T in V6. Subsequent autopsy revealed typical primary endocardial fibroelastosis.

The auscultatory findings were similar in both groups. The average heart rate of all

**Figure 2**

Electrocardiograms taken on a baby diagnosed clinically as having endocardial fibroelastosis. He improved steadily on digitalis therapy. The electrocardiogram as well as the heart size was normal at 6 years of age.
endocardial fibroelastosis

The age of onset of 41 postmortem-proved cases of primary endocardial fibroelastosis and in 33 cases identified clinically: 25 of the postmortem cases are from our own files, 16 cases are from the report of Kelly and Anderson.

cases on admission was between 160 and 170 beats per minute but ranged from 120 to 220 beats per minute. In moribund infants the heart sounds were of poor quality; tachycardia was common, but bradycardia occurred only occasionally.

Prior to death no murmurs were heard in 15 of the 25 postmortem cases of primary endocardial fibroelastosis. In 10 cases functional murmurs were heard: the murmurs in three of the cases were obviously functional, whereas in seven the murmurs could not be so identified until after repeated observations.

In the clinical group of 33 cases, 22 had no murmurs on examination at admission, eight had obviously functional murmurs, and three had probable functional murmurs. At the last examination, after observation for 2 to 8 years, it was obvious from the quality and variation of the murmurs that all of them were functional in origin.

was in the onset of signs and symptoms.

The one difference between the two groups They occurred a little earlier in the autopsied group; the age of onset in the two groups was almost entirely in the first 8 months of life (fig. 3).

Roentgenography
Radiologic evidence of cardiac enlargement was found in all cases. The average cardio-

thoracic ratio was 69 per cent, with a range of 58 to 75 per cent in the clinical group of cases, and 71 per cent, with a range of 56 to 80 per cent in the postmortem group; in the normal infant the cardiothoracic ratio rarely exceeds 55 per cent. Although the average heart size was similar in the two groups, only 14 per cent of the clinical group had a ratio greater than 70 per cent, whereas 64 per cent of the postmortem group had larger ratios.

On fluoroscopy left atrial enlargement, left ventricular enlargement, and poor cardiac action were noted in both groups. Except during acute congestive heart failure the lung fields appeared normal.

Electrocardiographic Findings

Rhythm
All cases had sinus rhythm except for the two cases in moribund children. Both these cases had conduction defects including prolonged P-R intervals, intermittent heart block, and wide QRS complexes. On admission, heart rates of all cases ranged from 120 to 220 beats per minute. There was no difference between

The age of onset of myocarditis in infancy and childhood is recorded in 79 cases reported in the literature and from our own files. Epidemics of myocarditis such as that reported by Freundlich et al. with a large number of cases concentrated in a short period of time were not included, since they appear to be isolated phenomena and do not present any problem in the differential diagnosis with endocardial fibroelastosis. Furthermore, all the cases reported by Freundlich were 6 months old or more at the time of onset.
the heart rates found in the clinical and the postmortem groups.

The P-R interval averaged 0.11 second (range 0.08 to 0.16 second) in the postmortem group; in the clinical group the average interval was 0.12 second (range 0.09 to 0.16 second). In 70 per cent of both groups P-R intervals ranged from 0.10 to 0.12 second.

The duration of the P waves averaged 0.05 second in both groups; the range was from 0.02 to 0.10 second. In 65 per cent the P-wave duration ranged from 0.04 to 0.07 second. There appeared to be no relationship between the P-wave duration or heart rate and the age of the infant, as is true in normal electrocardiograms.

The mean amplitude of the P wave in both groups was 2 mm. In the autopsied group the amplitude varied between 1 and 4.5 mm.; 35 per cent (eight cases) had abnormally tall P waves. Three of these cases had left atrial involvement and five had persistent congestive heart failure. In the clinical group the amplitude of the P wave varied from 1.0 to 3.5 mm., and six cases (14 per cent) had large P waves of more than 3 mm. In five of these cases the P-wave amplitude was abnormal following the initiation of therapy. In the sixth case the P wave was still 3 mm. high after 1 year, but it decreased to 1.5 mm. by the end of the second year of therapy.

The duration of the QRS interval averaged 0.06 mm. The range was similar in both groups and extended from 0.04 to 0.10 second. The average QRS duration in infancy of 0.055 second corresponds closely to the average found in our cases with endocardial fibroelastosis. In two cases the QRS interval was 0.10 second, but there was no other sign of bundle-branch block; Zeigler considered this to be prolonged for infancy.

Patterns of Electrocardiographic Hypertrophy Associated with Endocardial Fibroelastosis

Although the age, history, and clinical findings are essential for a diagnosis of endocardial fibroelastosis, the electrocardiogram is of dominant significance. It is characterized by a left loading pattern of increased voltage in the left ventricular precordial leads.

Of the 25 autopsied cases, three were in the terminal stages of illness, so that the electrocardiograms were difficult to interpret adequately. Two had evidence of right ventricular loading alone and a postmortem finding of endocardial fibroelastosis of the right ventricle. Such cases are very difficult or impossible to recognize clinically. There remained 20 cases in which there was evidence of left ventricular loading in the electrocardiogram, and one of these had evidence implicating both right and left ventricles. Thus, 19 of 22 cases remain (86 per cent) with a left loading pattern in the electrocardiogram.

In the autopsied group of cases showing left ventricular overload and left ventricular involvement at autopsy, 47 per cent had left loading diagnosed on the basis of the R wave in V6 of over 20 mm. as well as an S wave in V1 of over 20 mm. Only two cases (10 per cent) had left loading diagnosed on the basis of an S wave in V1 alone of 20 mm. or more. In three cases (17 per cent) left ventricular overloading was diagnosed on the basis of the ratio of the R/S in V1 being less than 0.8 at 12 months of age, or 0.2 between 12 and 24 months of age. Similar findings were noted by Vlad et al. On electrocardiographic study of their autopsied cases of endocardial fibroelastosis 78 per cent of the group had evidence of left ventricular loading; of these, 82 per cent had increased voltage in the pertinent precordial leads.

All the clinical cases in the present series demonstrated evidence of left ventricular loading either from the beginning of illness or once congestive heart failure was controlled. Three cases (9 per cent) showed right as well as left ventricular loading.

In a comparison of the clinical and postmortem groups (table 1) 17 per cent of the clinical group had electrocardiographic evidence of left ventricular overloading on the basis of the R wave in V6 over 20 mm., 66 per cent of cases had left ventricular loading diagnosed on the basis of the amplitude of the R wave in V6 as well as the depth of the S in V1 exceeding 20 mm., and only three cases (10 per cent) had left loading diagnosed on the bases of the depth of the S wave in V1 alone. In only two cases (7 per cent) left
loading was diagnosed on the ratio of R/S in V₁ alone. Thus 93 per cent had evidence of left ventricular loading on the basis of increased voltage in the precordial leads.

**T-Wave Direction in V₆**

The T-wave deflection in leads V₅ or V₆ was characteristically flattened or inverted in both postmortem and clinical cases initially, prior to the administration of digoxin (table 2). The two cases that did not have negative T waves in V₆ died suddenly, and repeated electrocardiograms were not taken. One clinical case had an upright T in V₆ initially but it became negative subsequently.

In the postmortem group the average depth of the T wave in V₆ was 1.5 mm., and in 75 per cent it was clearly inverted. The clinical cases had T waves that were a little deeper; the average depth was 2.5 mm., and in 95 per cent it was clearly inverted.

**Mean Electrical Axis and Direction of the Frontal Loop**

The mean electrical axis ranged in the postmortem cases from minus 10 to plus 110° and in the clinical cases from minus 10 to plus 100°. In both groups 77 per cent of the cases had a mean electrical axis in a range between plus 20 and plus 80°.

When it was possible to determine the direction of the frontal loop, it was clockwise in 96 per cent of the postmortem group and in 85 per cent of the clinical group. A counterclockwise loop was found in only six cases.

**History during Pregnancy**

In no case was there any evidence in the pregnancy history of an etiologic factor that might be related to endocardial fibroelastosis. Two mothers had difficulty with the later stages of pregnancy; one had toxemia and the baby had respiratory distress for a short time after delivery, and the other gave birth to a baby who appeared well initially. Kelly and Anderson also found no significant history of maternal illness in 17 autopsied cases.

**Birth Rank**

Data regarding birth order were available in 51 families. In both groups there was an increased probability of endocardial fibroelastosis with increasing birth rank.

**Birth Weight**

The average birth weight of the male and female cases was 3,246 and 3,133 Gm., re-

**Table 1**

<table>
<thead>
<tr>
<th>33 clinical cases</th>
<th>Endocardial fibroelastosis</th>
<th>19 postmortem cases</th>
<th>Myocarditis</th>
<th>23 cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tall RV₆ alone</td>
<td>17%</td>
<td>47%</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>Tall RV₆ and deep SV₁</td>
<td>66%</td>
<td>26%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Deep SV₁</td>
<td>10%</td>
<td>10%</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>Ratio R/S V₁ alone*</td>
<td>7%</td>
<td>17%</td>
<td>83%</td>
<td></td>
</tr>
</tbody>
</table>

* Abnormally low R/S ratio in V₁.

N.B. Vlad et al., 1953, 82 per cent of postmortem group (17), with LVH had increased voltage.

**Table 2**

<table>
<thead>
<tr>
<th>T-wave Amplitude in V₆</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroelastosis groups</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Myocarditis</td>
</tr>
<tr>
<td>T wave mm.</td>
</tr>
</tbody>
</table>

The magnitude of the T wave in precordial lead V₆ is compared in the clinical and postmortem groups of endocardial fibroelastosis with that in myocarditis.
respectively. Eighty per cent of both groups of cases had birth weights within the 10- to 90-per cent range. There were four cases that were premature by weight (2,180 to 2,450 Cm.).

Sex Ratio

In both groups females predominated slightly over males. This was only true in the absence of associated valvular disease; when the latter complication was present, males predominated.

Maternal Age

In both groups primary endocardial fibroelastosis occurred most often in infants born to mothers in the age group of 25 to 29 years. This age group corresponds to the peak incidence of childbirth in the general population. Analysis of the data, however, suggests that endocardial fibroelastosis did not occur so frequently in the older mothers as in the younger, despite the higher frequency of primary endocardial fibroelastosis with progressing birth rank. This suggested that the maternal age of mothers of children with primary endocardial fibroelastosis was significantly younger than in the general population ($p = 0.5$).

Familial Incidence

Data regarding siblings were available in 80 per cent of families. In six families multiple cases occurred. Thus, the presence of a known case of endocardial fibroelastosis in the family increases slightly the possibility of another occurrence. One of our cases that developed congestive heart failure in the newborn period was identified on this basis, despite an electrocardiogram that was not characteristic.

Discussion

Over the past 10 years we have been impressed with the clinical findings in babies of congestive heart failure, a large heart, no murmurs, and a distinctive electrocardiographic pattern. In such cases we have made a diagnosis of endocardial fibroelastosis, and in many instances the baby has died in the next few days and the diagnosis has been confirmed.

During the course of this study we observed a group of cases that responded initially to therapy. They were followed for several years. Five of them died during the course of the follow-up, 1 to 3 years after the original clinical diagnosis had been made. All five were found to have the typical endocardial lesion at autopsy.

One case not included in this series had been diagnosed as endocardial fibroelastosis in 1953 and responded well to therapy, with return of the heart size and electrocardiogram to normal. At the age of 7 years this child developed an unrelated attack of nephritis and died. At autopsy pearly white thickening of the endocardium of the left ventricle was readily seen and appeared similar to that seen in infants dying in the first year of life.

The problem in diagnosis involves differentiation of conditions in which congestive heart failure occurs in infancy unaccompanied by a significant heart murmur, and in which the electrocardiogram indicates a left ventricular overload. Idiopathic myocarditis and an anomalous left coronary artery arising from the pulmonary artery, calcification of the coronary arteries, glycogen-storage disease of the heart, medial necrosis of the coronary arteries, coarctation of the aorta, aortic stenosis, and mitral insufficiency are the chief defects that must be considered. Many of these lesions may be associated with a mild secondary endocardial fibrotic reaction that is, however, relatively insignificant when compared with the endocardium in the classical picture of primary endocardial fibroelastosis.

Anomalous Left Coronary Artery

Many reports have appeared in the literature of an anomalous left coronary artery arising from the pulmonary artery. A few cases survived into adult life but such individuals did not present signs or symptoms during infancy. Infants with this anomaly usually have a distinctive picture, the vast majority show signs and symptoms in the first 4 months of life, rarely before 2 months of age. The onset is that of heart failure, dyspnea, large liver, and, in a few cases, screaming or crying as if in pain.

Circulation, Volume XXIX, January 1964
ENOCARDIAL FIBROELASTOSIS

The electrocardiogram is very helpful in making the differential diagnosis. All of the cases of anomalous coronary from the pulmonary artery that develop congestive failure in infancy eventually show the ischemic pattern of myocardial infarction. This change is associated with a left ventricular loading pattern usually of the type that produces a deep S in V₁ rather than a tall R in V₆. Characteristically, there is a deep Q wave in leads I, aV₃, and in V₅ and V₆. The S-T segment in V₅ and V₆ is elevated distinctly in the majority of cases, although it may be depressed. The pattern is that of an anterolateral myocardial infarction. While the electrocardiogram is almost invariably diagnostic, confirmatory evidence can be obtained from an aortogram with the tip of the catheter in the region of the coronary arteries. This will reveal a large, completely filled right coronary artery arising from the aorta, and will show an absence of left coronary arising from the aorta, indicating its anomalous presence elsewhere.

The cases of anomalous left coronary artery arising from the pulmonary artery that develop heart failure in infancy, almost without exception are dead by the end of the first year of life. It is obvious, therefore, that a group of 33 clinically diagnosed cases of endocardial fibroelastosis that survived cannot have been cases of this anomaly. It should be noted that the number of cases of anomalous coronary arising from the pulmonary artery have a mild, pallid degree of endocardial fibroelastosis of the left ventricle at postmortem examination, which is obviously a secondary phenomenon and does not rival the dense lesion of primary endocardial fibroelastosis.

Calcification of the Coronary Arteries

Calcification of the coronary arteries in infancy is associated with widespread calcification of the arteries throughout the body and may involve the renal and thyroid vessels, and the arteries of numerous other vital organs. In the majority of cases these infants die because of the general arterial involvement rather than the specific effect on the heart, but occasionally congestive heart failure may occur and produce an electrocardiographic pattern similar to that found in endocardial fibroelastosis. Thus, the clinical picture, the electrocardiographic findings, and the calcification of the coronary arteries may at times be indistinguishable from primary endocardial fibroelastosis. Although this condition must be considered in the differential diagnosis, it apparently does not represent a real problem, since it is so rare. It is uniformly fatal and does not respond to digitalis. X-ray of the various portions of the body may reveal calcification of the arteries and thus lead to the correct diagnosis.

Glycogen-Storage Disease of the Heart

Glycogen-storage disease of the heart is a uniformly fatal disease in infancy, and death usually occurs during the first 8 months of life. The electrocardiogram may show left ventricular loading with T-wave inversion in V₆. The majority of these children have a history of generalized muscular weakness from birth, and characteristically have macroglossia. A histologic section from an involved muscle may reveal the true diagnosis.

Myocarditis

The problem of differential diagnosis between endocardial fibroelastosis and the various lesions and anomalies that may simulate it in infancy is usually clarified by observation for a week or two, and by taking several electrocardiograms. In the present series of 33 cases all were followed for 2 to 8 years, thus making it virtually certain that the simulating anomalies were ruled out. One problem of myocarditis remains, however. A review of the clinical findings and especially the electrocardiogram indicates that the differentiation between endocardial fibroelastosis and myocarditis can usually be made during life.

The pattern of age of onset in myocarditis differs somewhat from that of endocardial fibroelastosis. Recent literature demonstrates that Coxsackie myocarditis, when it occurs in the mother at the end of pregnancy, is likely to produce the same infection in the newborn baby and will almost invariably be associated with myocarditis with a mortality of approxi-
mately 70 per cent. After the first month of life the incidence of myocarditis with Coxsackie infection falls precipitously, and the mortality becomes very low. After the neonatal period myocarditis appears to be scattered irregularly through the pediatric age group and is not concentrated in any particular year (fig. 4). On the other hand, in endocardial fibroelastosis the age of onset is in the first 8 months of life in 85 per cent of cases (fig. 3). In myocarditis, on the other hand, if one rules out the Coxsackie virus infections in the neonatal period, only 30 per cent have their onset in the first 8 months of life.

The electrocardiograms in myocarditis and endocardial fibroelastosis show differences of diagnostic significance. The voltage of the R wave in V₆ or the voltage of the S wave in V₁ is abnormally high in most cases of endocardial fibroelastosis; it is rarely increased in myocarditis (table 1). The R wave in V₆ is abnormally high in most cases of endocardial fibroelastosis; it is rarely increased in myocarditis. The T wave in V₆ is more deeply inverted in endocardial fibroelastosis than in myocarditis in most cases, and it tends to be flat or slightly inverted in the myocarditis group (table 2). A pattern of myocardial infarction may be seen in 10 per cent of children with myocarditis but is very rare in endocardial fibroelastosis. A Q wave in V₆ of 1 mm. or greater is seen in 60 to 70 per cent of the cases of endocardial fibroelastosis, but a Q wave in V₆ is uncommon in myocarditis unless a pattern of myocardial infarction is present (table 3).

Eighty-five per cent of the cases of endocardial fibroelastosis have a left loading pattern, and 93 per cent of these also have an increase in voltage in the leads pertaining to the left ventricle. On the other hand, in myocarditis only 7 per cent of cases showed an increase in voltage in the same leads, and any left loading present is associated with a simple lowering of the R/S ratio in V₁. This striking difference provides security of diagnosis in cases showing the characteristic clinical and electrocardiographic picture. As a result, all of the autopsy-proved cases (20) that showed this pattern were diagnosed correctly during life, and myocarditis was correctly ruled out.

One may not always reach the correct diagnosis, since an occasional case of myocarditis may have a left loading pattern with increased voltage of S in V₁ or R in V₆. This is an uncommon finding, and we have not been misled in this manner to date. An occasional case of endocardial fibroelastosis may show a low voltage pattern similar to that seen in myocarditis. This occurrence does not, however, invalidate the statement that all cases that satisfied the criteria and came to autopsy had endocardial fibroelastosis.

In the majority of cases with myocarditis the diagnosis was correctly identified from the clinical findings and the electrocardiogram. Confirmation was subsequently obtained at autopsy. None of our cases of myocarditis was considered to be endocardial fibroelastosis during life. We have encountered one case with endocardial fibroelastosis that was considered to be myocarditis because of the low voltage in the electrocardiogram. An autopsy revealed the correct diagnosis.

Recently Décourt and co-workers reported on a punch-biopsy study of the heart. Fifteen patients had clinical evidence of endocardial fibroelastosis and the presence of this lesion was confirmed in each case by biopsy of the endocardium. These children are doing well.

### Table 3

**Incidence of Q waves in Precordial Lead V₆ in Endocardial Fibroelastosis and Myocarditis**

<table>
<thead>
<tr>
<th>Endocardial fibroelastosis</th>
<th>Myocarditis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postmortem</td>
<td>Clinical</td>
</tr>
<tr>
<td>0</td>
<td>37%</td>
</tr>
<tr>
<td>0.5—1 mm.</td>
<td>4%</td>
</tr>
<tr>
<td>1+ mm.</td>
<td>59%</td>
</tr>
</tbody>
</table>

* Three fourths of this figure were q₆ due to myocardial infarction pattern.

### Endocardial Fibroelastosis Associated with Valvular Involvement

The cases with valvular involvement were excluded from the main body of this study because it is difficult to be certain about the type and origin of the valvular pathology.
ENDOCARDIAL FIBROELASTOSIS

There may well be an intimate relationship between the mural endocardial fibroelastic reaction and the pearly white thickening of the mitral valve. This combination was regarded as primary endocardial fibroelastosis by Kelly and Anderson.6 In the course of our study we encountered 11 such cases at autopsy: 10 had mitral valve involvement as well as the typical endocardial lesion, and six of these also had a similar process imposed on the aortic valve. The eleventh case had aortic valve involvement without the mitral lesion.

Seven of the 11 cases showed a left ventricular overload pattern in the electrocardiogram. Of those cases that did not show left loading, three had evidence of right ventricular overload and one electrocardiogram recorded in a moribund child was difficult to assess. One of the cases showing right ventricular overload had aortic stenosis, mitral stenosis, and endocardial fibroelastosis with a nondilated left ventricle. The remaining two cases showed right ventricular overloading and were found to have mitral valve involvement at autopsy.

Among the 11 cases all but one had flat or inverted T waves in V6. The case with the upright T in V6 was the one with aortic stenosis as an isolated valvular involvement associated with endocardial fibroelastosis of the left ventricle.

The seven cases with left ventricular loading had an increased amplitude of R in V6 in two, a tall R in V6 and a deep S in V1 in two, and a deep S in V1 alone in one. In two cases the only evidence of left ventricular overload was as in inversion of the T wave in V6. Both of these cases were in severe congestive heart failure at the time the electrocardiograms were taken, which may account for the absence of increased voltage.

One may suspect the presence of endocardial fibroelastosis in a baby with congestive heart failure and a systolic murmur in the first year of life with inverted T waves over the left precordium, with or without increased voltage of the R in V6 or the S in V1. In the face of the murmurs that go with these valvular lesions one cannot make the diagnosis with accuracy, since isolated aortic stenosis or large intracardiac left-to-right shunts may at times give similar electrocardiographic findings.

We did not encounter any infants who had evidence of involvement of the pulmonary or tricuspid valve associated with the endocardial lesion. Kelly and Anderson6 had two cases with an involvement of the tricuspid valve; some degree of involvement of all four chambers was noted in 15 of their 17 cases. At the same time they indicated that the left ventricular or the left atrial lesions were usually more marked and obvious.

Kelly and Anderson demonstrated that all but two of their 17 cases had dilated hearts, an incidence that was confirmed in our autopsy-proved material. They referred to these two cases as having an absence of dilatation, whereas Edwards used the term "contracted left ventricle." It would seem more suitable to designate them as nondilated as the former authors do, since such hearts are hypertrophied and somewhat enlarged. One of our cases, as was mentioned above, fell into this category and was associated with aortic and mitral valve involvement. It is generally recognized that some cases of aortic stenosis may have marked hypertrophy of the left ventricle without significant chamber enlargement. This type of myocardial response would not be expected to give right ventricular loading in the electrocardiogram. The cause of such loading may be related more to the advanced stage of congestive heart failure than has been recognized until now. It has been our experience that the right ventricular loading pattern in such cases changes quickly to a left loading one if the baby survives under treatment. The contracted left ventricle of aortic or mitral atresia is an entirely different entity.

Since the present study was begun, Noren et al.16 and Ainger (quoted by Noren) have presented preliminary studies on the use of a mumps antigen skin test in primary endocardial fibroelastosis. They have found a high incidence of positive reactions in their clinically diagnosed cases and a very low incidence in the normal infant. While their emphasis was on etiology, to us this appears to offer a test
of some diagnostic significance and we have, as a result, skin tested 31 cases of primary endocardial fibroelastosis that satisfied the diagnostic criteria set forth in this paper. Many were children included in this study and now are available for skin testing up to 9 years after the onset of symptoms. The age at skin testing of these was as follows: under 1 year, 6; 1 to 2 years, 3; 2 to 5 years, 6; 5 years and over, 16.

Among the total of 31 cases of clinically diagnosed primary endocardial fibroelastosis, 24 had a positive skin test, two were negative, and five were doubtful. The doubtful or negative cases were all in the 5-year-or-over age group. The blood sera of the patients with positive skin tests were uniformly negative in the under-2-year age group. The one positive serum was in an older child.

We skin tested 104 infants and children who were in the hospital for a variety of other conditions (77 had congenital heart disease). Seven of these were positive and all of them were 5 years of age or older. The sera of most cases with positive skin tests were tested for mumps virus antibodies; one was positive.

Thus, the mumps skin test antigen was positive in all cases with clinical primary endocardial fibroelastosis tested under the age of 5 years. These findings are similar to those of Noren and Ainger.

The mumps antigen skin test, therefore, appears to be a most useful diagnostic procedure in the age group under 2, when primary endocardial fibroelastosis has its characteristic onset in the pediatric age group. The reason for this positive reaction in these cases does not seem clear at the present time, since it appears to be most frequently associated with a lack of antibodies in the sera to mumps. Further study of this problem is necessary but it would appear likely that the mumps antigen skin test should be considered one of the useful criteria for diagnosis in the first 2 years of life.

The skin test will prove helpful in three particular categories: 1. In augmenting our criteria for the diagnosis of primary endocardial fibroelastosis. 2. When the criteria for diagnosis listed above are not quite adequately fulfilled and there is some doubt about the diagnosis. 3. When an infant under 2 years of age has an organic murmur originating in the mitral or aortic valve associated with failure and left ventricular loading in the electrocardiogram, a positive skin test would provide strong additional evidence of underlying primary fibroelastosis.

**Summary**

A comparison has been made of the clinical features of a group of autopsy-proved cases of endocardial fibroelastosis and a clinically diagnosed group with similar findings. It has been possible to make a diagnosis of endocardial fibroelastosis before death in all cases showing a characteristic clinical and electrocardiographic pattern. The characteristic features are (a) appearance of congestive heart failure; (b) absence of organic heart murmurs; (c) onset of signs or symptoms in the first 8 months of life (85 per cent) and rarely after 1½ years; (d) a period of observation under therapy during which is ruled out the conditions that simulate endocardial fibroelastosis, such as an anomalous coronary artery arising from the pulmonary artery, glycogen-storage disease, coronary artery necrosis, or myocarditis; (e) an abnormal increase in voltage of R in V₆, S in V₁, or both together; (f) a flat or inverted T wave in V₆ (85 per cent have a T wave 1 mm. or deeper); (g) a Q wave in V₆ (present in 60 per cent).

All the cases proved at autopsy that fulfilled these criteria during life were correctly diagnosed before death. Approximately 85 per cent of the total group were thus recognized. Fifteen per cent were not identified because electrocardiographic tracings showed an atypical right loading pattern. An occasional case with right loading may be suspected by history of a previous sibling with endocardial fibroelastosis.

Since the differential diagnosis between endocardial fibroelastosis and acute myocarditis has been considered difficult in the past, a group of infants and children with myocarditis were reviewed. The majority were proved at autopsy. Such children were also correctly diagnosed during life in most instances.
patients who were diagnosed clinically as having endocardial fibroelastosis and who survived had electrocardiographic patterns that were similar to those in the autopsy-proved group and unlike those in the myocarditis group. The chief differences were in voltages of R and S waves in precordial leads V₆ or V₅, T waves in V₆ and Q waves in V₆.

Cases of endocardial fibroelastosis associated with mitral or aortic valvular disease usually had a similar age of onset or a little earlier. The electrocardiographic pattern was similar. The presence of an aortic or mitral systolic murmur made it difficult to be certain about the underlying pathology. The left loading pattern, however, with increased voltage in the pertinent precordial leads accompanied by a flat or inverted T wave in V₆ in a baby with a large heart or with congestive heart failure, provides suggestive evidence of endocardial fibroelastosis.

The contracted type of endocardial fibroelastosis reported by Edwards is a relatively rare finding. When it does occur, it may or may not be associated with a right loading pattern in the electrocardiogram. The right loading pattern in endocardial fibroelastosis is more likely to be due to heart failure with pulmonary congestion and overloading of the right ventricle, which in an infant may then overshadow the left. This pattern may revert to the more characteristic one of left loading after digitalization has been completed.

The mumps antigen skin test is proving to be a useful diagnostic tool, since it is found to be positive in primary endocardial fibroelastosis in the first 2 years of life. In our experience this occurs without a positive serum antibody reaction to mumps virus. Normal children, or those with congenital heart disease in the same age group, rarely have a positive skin reaction unless they have a recent history of mumps. Further work is needed to clarify this relationship, but on the evidence to date its diagnostic value in primary endocardial fibroelastosis shows considerable promise.

References
The Diagnosis of Primary Endocardial Fibroelastosis
FRANK J. SELLERS, JOHN D. KEITH and JAMES A. MANNING

Circulation. 1964;29:49-59
doi: 10.1161/01.CIR.29.1.49
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1964 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/29/1/49

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/