ELECTROCARDIOGRAPHIC FINDINGS IN LEUKEMIA

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ALTHOUGH leukemic infiltrations of the heart are often encountered, particularly in the stem cell and myelogenous types of leukemia, little attention in the literature has been given to their clinical recognition. Cardiac manifestations, almost always first discovered at necropsy, have been considered to be a part of the protean nature of the leukemic process and not a complication of the disease itself. However, occasionally symptoms produced by myocardial infiltrates have been the first or the most outstanding findings early in the course of the disease. Wintrobe and Mitchell, in discussing atypical manifestations of leukemia, reported 2 such instances. One patient was treated for "heart disease" due to paroxysmal tachycardia and precordial discomfort for several months before myeloid leukemia was diagnosed. The other was a patient in whom the diagnosis of gallbladder and coronary diseases was made, and only at the autopsy was it found that the patient had a myeloid chloroma with widespread infiltrations. A 15 year old girl with a massive pericardial effusion as the most outstanding manifestation was later found to have a lymphatic leukemia with infiltration into the myocardium and pericardium. Willius and Amberg reported leukemic infiltration of the myocardium in a 2½ year old boy, in whom the main symptom of dyspnea could not be accounted for solely by the moderate secondary anemia which he manifested.

In reviewing 123 fatal instances of leukemia (0.86 per cent of 14,400 consecutive autopsies), Kirshbaum and Preuss found that leukemic infiltration of the heart occurred in 43 of the cases (34 per cent). In 7 of these, the wrong clinical diagnosis of either rheumatic or arteriosclerotic heart disease had been made. An interesting case report of a patient with myelogenous leukemia was that of Blotner and Sosman. Their patient had a 2:1 A-V block which was treated with x-ray therapy applied directly to the heart area causing temporary disappearance of the block.

The multiplicity of symptoms displayed by leukemic involvement of the heart is determined by the location and extent of the infiltrations and the commonly associated myocardial hemorrhages. So, one may note various disturbances of the cardiac rhythm or symptoms of congestive heart failure. Since anemia may also cause weakness, palpitation, and dyspnea, since tachycardia may occur with the elevated basal metabolism often associated with leukemia, and since ascites may be due to either enlargement of the spleen or peritoneal involvement, these symptoms by themselves are not sufficient to make the diagnosis of cardiac infiltrations.

Early recognition of involvement of the heart, due to either leukemic infiltrations or to multiple small myocardial hemorrhages, with the prompt exhibition of the therapeutic measures commonly used in the treatment of heart failure, may
afford the patient some relief from troublesome symptoms. Therefore, a review was undertaken to ascertain if the electrocardiogram might be of aid in making a diagnosis of leukemic involvement of the heart.

The following is a correlation of the electrocardiograms, autopsy findings, and clinical course of 8 patients with leukemia. Only pertinent data will be presented. In 5 patients, electrocardiograms were taken less than one month before death, and in the 3 others electrocardiograms were taken five weeks, two months, and seven months respectively before their death. Autopsy studies were made by one of us without knowledge of the histories or electrocardiographic interpretations. The electrocardiograms were interpreted before obtaining information of the clinical course or the autopsy results. Finally, the amassed material was examined for possible correlations.

CLINICAL DATA

The ages of these 8 patients ranged from 3 to 55 years. Four cases were diagnosed as lymphatic leukemia, 2 as blast or stem cell leukemia, and 2 as myelogenous leukemia. All of the patients had anemia with red blood cell counts varying between 810,000 and 3,500,000.

Five patients had clinical signs of either right or left heart failure. In all of these, physical examination revealed enlargement of one or more chambers of the heart. In the 3 instances where chest x-rays were made, the cardiac enlargements were confirmed. Three of the 5 patients had either systolic or diastolic murmurs or both.

Except for an apical systolic murmur in 1 instance, no clinical evidence of heart disease was present in the other 3 patients (see electrocardiograms, fig. 2 B, C, and D). Electrocardiograms of these 8 patients are shown in figs. 1 and 2.

ELECTROCARDIOGRAPHIC INTERPRETATIONS

Figure 1A, taken twenty-five days before death, shows a sinus tachycardia with an occasional ventricular premature systole (not shown in the record). S-T is depressed and T is small in all of the leads. T is diphasic in 1, 2, and the chest leads. QRS is upright in lead CF2. The interpretation is: sinus tachycardia, ventricular premature systoles, probably combined heart strain, a definitely abnormal record.

Figure 1B, taken two weeks before death, shows a prolongation of the P-R interval to 0.24 second. R4 is tall and S2 and S3 are deep. S-T1 is depressed and S-T3 is elevated. T1 is diphasic. QRS in lead CF3 is polyphasic. S-T is depressed in leads CF4 and CF5. T is diphasic in lead CF4 and inverted in lead CF5. The interpretation is: sinus rhythm, first degree A-V block, left heart strain, a definitely abnormal record.

Figure 1C, taken sixteen days before death, shows a tiny and diphasic QRS in lead 2. The T waves in leads CF2 and CF4 are inverted. The interpretation is: sinus rhythm, left axis shift, a definitely abnormal record.

Figure 1D, taken 20 days before death, shows a sinus tachycardia. QRS is small in lead 1; there is depression of the S-T segments, and the T waves are small in all of the limb leads. S-T is depressed in lead CF4 and T inverted in leads CF2 and CF4. The interpretation is: sinus tachycardia, a definitely abnormal record.

Figure 2A, taken seven months before death, shows a QRS1 which is mainly
inverted with a deep S wave. S-T is depressed in leads 1 and 2 and T is inverted in leads 2 and 3. The T inversions in the chest leads may be normal for a patient of this age (6 years). The interpretation is: sinus tachycardia, right axis shift, possibly right heart strain, a definitely abnormal record.

Figure 1B, taken ten days before death, shows a sinus tachycardia. A small Q wave is present in lead 3. The T waves are small in the limb leads. The inversion of the T waves in leads CF2 and CF4 may be normal for a child (3 years old). The interpretation is: sinus tachycardia, a borderline record.
Figure 2C, taken two months before death, shows depression of the S-T segments in all of the limb leads. T\textsubscript{2} is diphasic and T\textsubscript{3} inverted. The T wave changes in CF\textsubscript{2} and CF\textsubscript{4} could be normal for the age of this patient (3\frac{1}{2} years). The interpretation is: sinus tachycardia, right axis shift, a definitely abnormal record.

Figure 2D, taken five weeks prior to death, shows a sinus tachycardia. A small Q wave is present in leads 2 and 3 and S-T is depressed in these leads. The T wave changes in the chest leads could be normal for a child of this age (4\frac{1}{2} years). The diagnosis is: sinus tachycardia, a borderline record.
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In summary, all of the electrocardiograms except iB and iD were interpreted as definitely abnormal records. The 2 exceptions were interpreted as borderline records. All the electrocardiograms taken on those patients with clinical evidence of heart disease were definitely abnormal. Contrariwise, the only 2 records which were not interpreted as definitely abnormal were taken on 2 of the 3 patients without clinical manifestations of cardiac involvement.

AUTOPSY FINDINGS

Postmortem examination was performed on all of the 8 patients. In 4 of them, leukemic infiltrates were noted in the various layers of the heart and particularly in the myocardium. These patients were among the 5 which presented signs of cardiac failure. (Fig. 3 shows a representative section from this group.)

In the 4 others, the small vessels of the myocardium were engorged with immature white cells. In 2 instances this capillary engorgement was associated with recent small foci of interstitial hemorrhages, and severe fatty degeneration was noted in another patient of this group. The latter had clinical evidence of left heart failure. (Fig. 4 shows a representative section from this group.)

No noteworthy arteriosclerotic changes were present in the coronary arteries of the 2 patients who were 55 years of age.

Correlation Among Clinical, Electrocardiographic, and Autopsy Findings

The patients represented in electrocardiographic illustrations iA, iB, iC, and 2A all had clinical evidence of heart failure with cardiac enlargement, and definitely
abnormal electrocardiograms. In these patients, autopsy examination revealed myocardial infiltrates. Therefore this group shows a close correlation between all methods of examination.

A fifth patient (electrocardiographic illustration 1D) had a large globular heart with “tigering” and fragmentation of myocardial fibers. Engorgement of the capillaries was noted, but no leukemic infiltrations of the heart layers were found. The electrocardiographic changes were nonspecific. The remaining 3 patients (electrocardiographic illustrations 2B, 2C, and 2D) had no clinical evidence of heart disease. In none of these were cardiac infiltrations noted, but the capillaries of the heart were engorged by leukemic cells in all instances. Again in this group of 4 patients, the clinical findings were confirmed by the autopsy evidence. The electrocardiographic abnormalities could be explained by the marked anemia and possible superimposed myocardial ischemia due to occlusion of the capillaries of the heart by leukemia cells.

The changes in the electrocardiogram depend upon the extent and location of the myocardial infiltrates. Similar electrocardiographic aberrations may occur, owing to unrelated conditions such as arteriosclerotic heart disease and transitory coronary insufficiency in older patients. Whenever the electrocardiogram is abnormal in a patient with leukemia, a careful search should be made for clinical evidence of heart disease. At times, the electrocardiogram may be the first evidence of myocardial infiltrates. It should be recalled that infiltrations of the heart are common in leukemia (34 per cent in one large series of autopsied cases) and many varieties of heart disease may be simulated.
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CONCLUSIONS

1. The heart is frequently involved in leukemia.
2. There is a close correlation between the presence of leukemic myocardial infiltration, signs of heart disease, and abnormalities of the electrocardiogram.
3. The electrocardiographic changes do not constitute a diagnostic pattern.

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