Frequency of Cerebral Infarction in Patients With Inherited Neuromuscular Diseases

José Biller, MD, Victor Ionasescu, MD, Hans Zellweger, MD, Harold P. Adams Jr., MD, and Deborah T. Schultz, RN, BSN

We evaluated the frequency of cerebral infarction in 131 patients with Duchenne’s muscular dystrophy, myotonic dystrophy, Becker’s muscular dystrophy, or Friedreich’s ataxia. Electrocardiographic abnormalities were found in 83% of patients with Duchenne’s muscular dystrophy, 56% with myotonic dystrophy, 50% with Becker’s muscular dystrophy, and 25% with Friedreich’s ataxia. Atrial flutter occurred in 2.3% of the patients, and atrial fibrillation in only 0.9%. Evidence of cerebral infarction was found in only 2 patients (1.5%). Both patients had cardiomyopathy and either atrial fibrillation or flutter. Despite frequent cardiac involvement, cerebral infarction is an uncommon occurrence in patients with inherited neuromuscular diseases. (Stroke 1987;18:805–807)

Numerous observations of cardiac abnormalities have been described in patients with inherited neuromuscular disorders. Cerebrovascular problems, on the other hand, have received little attention. We present the results of our prospective observations in a group of 131 patients with selected inherited neuromuscular diseases followed by the Division of Medical Genetics at the University of Iowa between 1968 and 1985.

Subjects and Methods

One hundred thirty-one patients with either myotonic dystrophy (MyD), Duchenne’s muscular dystrophy (DMD), Becker’s muscular dystrophy (BMD), or Friedreich’s ataxia (FA) attending neuromuscular clinics sponsored by the Division of Medical Genetics, University of Iowa Hospitals and Clinics, between 1968 and 1985 were studied. The University of Iowa Hospitals and Clinics serve as the state of Iowa’s comprehensive tertiary health care center and serve primarily the state of Iowa and the northwestern part of Illinois. All patients were seen by coinvestigators every 6 months for a minimum of 3 years and a maximum of 17 years. All patients were referred by other physicians (neurologists, pediatricians, geneticists, and family practitioners). The patients were seen in either Iowa City or in one of 10 field clinics close to the homes of severely handicapped patients or patients without transportation. Data were entered into the files of the Division of Medical Genetics. The clinical course, electrocardiograms (ECGs), chest x-rays, and outcomes were analyzed in all patients.

Results

We screened 157 patients; 26 were lost to follow-up primarily because of moving to other parts of the United States. The remaining 131 patients serve as the basis for this report. There were 102 males and 29 females ranging in age from 6 to 60 years, with a mean age of 21.3 years; 88% came from the state of Iowa, 12% from neighboring states (Illinois, Wisconsin, Minnesota, Missouri, Nebraska, and South Dakota). For comparison, our patients were divided into 4 groups: Group 1 (DMD), Group 2 (MyD), Group 3 (BMD), and Group 4 (FA). Our results are summarized in Table 1. Atrial flutter was found in 3 patients with MyD and in 1 with DMD. Atrial fibrillation occurred in only 1 patient with FA. Cerebral infarction was diagnosed in 2 (1.5%) of 131 patients. Both patients with stroke had a symptomatic cardiomyopathy and either atrial fibrillation or flutter; one had MyD and the other had FA. We attributed the cerebral infarction to embolism from a cardiogenic source in both cases. The 2 patients who sustained cerebral infarction are detailed below.

Patient Histories

Case 1 (Group 4). A 27-year-old man presented to the hospital with right-sided weakness and drowsiness. At 11:00 AM on the day of admission, his father found him slumped over in his wheelchair, unresponsive, with his head and eyes deviated to the left. He was known to have FA, diagnosed at age 10. He had been wheelchair-bound since the age of 17. He had atrial fibrillation and a cardiomyopathy since the age of 24.

His blood pressure was 102/70 mm Hg, pulse 80 and irregularly irregular, respiratory rate 18 breaths/min, and temperature 37°C. General physical examination was remarkable for severe kyphoscoliosis and mild pes cavus deformities bilaterally. There was a broad and inferolaterally displaced apical impulse. The cardiac rate was irregularly irregular. There was a loud S1 and S2, but no murmurs. He was drowsy but arousable. He...
Table 1. Summary of 131 Patients With Inherited Neuromuscular Diseases

<table>
<thead>
<tr>
<th></th>
<th>Duchenne's muscular dystrophy</th>
<th>Myotonic dystrophy</th>
<th>Becker's muscular dystrophy</th>
<th>Friedreich's ataxia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>52</td>
<td>61</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>32 males, 29 females</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>Ages</td>
<td>6–28 years</td>
<td>13–60 years</td>
<td>8–40 years</td>
<td>9–27 years</td>
</tr>
<tr>
<td>Mean age</td>
<td>12.2 years</td>
<td>33.1 years</td>
<td>25.1 years</td>
<td>15 years</td>
</tr>
<tr>
<td>Abnormal ECGs</td>
<td>43 (83%)</td>
<td>Most had conduction abnormalities; 4 arrhythmias: 3 atrial flutters, 1 atrial premature beats</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>34 (56%)</td>
<td>No arrhythmias</td>
<td>7 (50%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 arrhythmia: 1 atrial fibrillation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of strokes</td>
<td>0</td>
<td>1 (1.6%) cardioembolic cerebellar infarct</td>
<td>0</td>
<td>1 (25%) cardioembolic left cerebral infarct</td>
</tr>
</tbody>
</table>

had no verbalizations. There was a left gaze preference and right-sided hemiparesis. There was generalized areflexia and bilateral extensor plantar responses. Coordination and sensation could not be tested. Computed tomography (CT) scan demonstrated a large left temporal-parietal infarct. Chest x-ray showed cardiomegaly and marked thoracic scoliosis with a curve convex to the right. An ECG revealed atrial fibrillation. Echocardiogram revealed asymmetric septal hypertrophy without obstruction, infiltrative cardiomyopathy, left atrial enlargement, and reduced left ventricular systolic function. He received i.v. heparin followed by oral anticoagulants. The patient remains aphasic, hemiparetic, and wheelchair-bound in a nursing home 2 years after hospital discharge.

CASE 2 (GROUP 2). A 55-year-old man presented to the hospital with headaches, nausea, vomiting, and inability to walk. He was known to have MyD and congestive heart failure. The night before admission, he suddenly developed occipital headaches and noticed that he could not get out of his chair where he was watching television. He complained of nausea and vomited several times.

His blood pressure was 100/60 mm Hg, pulse 72, respirations 18 breaths/min, and rectal temperature 37.1°C. Cardiac examination revealed inferolateral displacement of the apical impulse and a Grade II/VI systolic murmur at the apex without radiation. He had the classical features of MyD, dysarthric speech and left-sided hemiataxia. CT scan showed a left cerebellar infarct. Chest x-ray demonstrated cardiomegaly and a right lower lobe infiltrate. An ECG revealed atrial flutter and left bundle branch block. Echocardiography disclosed left ventricular and left atrial enlargement and poor left ventricular function. Left ventricular ejection fraction was 16%. Hospital course was complicated by pulmonary edema, profound bradycardia, hypotension, and asystole, culminating in the patient's death 8 weeks after the onset of stroke.

Postmortem examination showed dilated cardiomegaly and normal pericardial and epicardial surfaces. The endocardial surface was free of vegetations or thrombi. There were no anomalies of the atria, ventricles, valves, venous return, or great arteries. The coronary arteries were normal. Microscopic examination of the heart revealed increased fibrous tissue interposed between healthy fibers, a focal microscopic infarct in the papillary muscle, and focal fatty infiltrates. There were minimal variations in the size and shape of the cells and their nuclei. Findings in other organs outside the central nervous system included a scarred infarct of the right kidney, chronic passive congestion of the liver, congestion and edema of the lungs, lipid pneumonia, and testicular atrophy. Examination of the brain showed generalized ventricular enlargement and a brown-stained infarct involving the inferior aspect of the left lateral cerebellar hemisphere, measuring approximately 1.0 × 1.5 cm on the surface and extending 3.0 cm into the cerebellar cortex and white matter more laterally. Microscopic sections demonstrated a subacute cerebellar cortical infarct overlying the dentate nucleus, which was mildly gliotic and contained fewer than normal neurons. Paraffin sections of the psoas muscle showed focal variations in fiber size associated with an increased number of internal nuclei. Occasional necrotic fibers were also present.

Discussion

Cardiac involvement is well documented in different inherited neuromuscular conditions.1–12 Waters11 reported a high incidence of cardiac abnormalities in DMD, BMD, and MyD, and nearly 100% involvement in FA. The severity of heart involvement varies greatly. Perloff10 suggested that cardiac disease is seldom serious in MyD but may be life threatening in DMD or FA. In spite of the frequent cardiac involvement, many of these patients are without symptoms. This is partly explained by the limited cardiac load imposed by the immobilization created by the underlying neuromuscular process. ECG abnormalities do not always indicate cardiomyopathy.3 Diagnostic difficulties are often encountered in the interpretation of the tracings secondary to the frequent coexistent skeletal deformities.

The importance of embolism of cardiac origin to the cerebral circulation has become increasingly recognized in recent years. The prevalence of cerebral infarction in our study was low (1.5%) considering the frequency of cardiac involvement. However, it occurred in half of the patients who developed atrial
fibrillation or atrial flutter. Both patients had an underlying symptomatic cardiomyopathy associated with congestive heart failure and atrial flutter or fibrillation. We attributed infarction to cardiogenic cerebral embolism. Both patients had advanced cardiomyopathy, left atrial enlargement, impaired left ventricular function, and paroxysmal atrial flutter or atrial fibrillation. The development of atrial fibrillation or atrial flutter usually signifies, as with many other cardiomyopathies, severe myocardial damage and clinical deterioration. One patient suffered a large left middle cerebral artery infarct and has remained aphasic and hemiplegic for 2 years. Another patient with a left posterior inferior cerebellar artery territory infarct suffered rapid cardiac deterioration and died within 8 weeks of his stroke.

Although patient groups that are weighted with individuals early in the course of the disease may be quite different from those that are weighted with individuals who have had the disease for a long time, our study demonstrates that in contrast with the frequent cardiac involvement, cerebral infarction is an uncommon occurrence in patients with MyD, DMD, BMD, and FA. Our results suggest that advanced cardiomyopathy associated with atrial fibrillation or atrial flutter increases the risk of cerebral embolism and clinical deterioration in these patients.

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References

Key Words • cerebral infarction • inherited neuromuscular diseases
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