Atrioventricular Block and Supraventricular Arrhythmias with X-linked Muscular Dystrophy

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SUMMARY This report describes a family showing muscular dystrophy and atroventricular block with an x-linked hereditary transmission. Among a known pedigree of 101 family members, 12 males were found to have skeletal muscle involvement and six needed pacemakers around age 30 years. Unlike the x-linked muscular dystrophies of Duchenne and of Becker, the predominant skeletal involvement was in humeral muscles, was usually very mild, and did not produce incapacitation. Cardiac involvement consisted of various atrial arrhythmias and atrioventricular block. The few sporadic reports of other families that describe the same disease under different names are briefly reviewed. Recognition of this subtle muscular dystrophy is important for early detection of incipient complete atrioventricular block to prevent fatal complications by pacemaker insertion.

IN THIS REPORT we present a large family in which several male members required cardiac pacemakers for atrioventricular block. The cardiac problem was found to be associated with a peculiar and occasionally very subtle skeletal myopathy inherited as an x-linked recessive trait. We believe that this disease, although unusual, is more common than has been recognized and detection of affected male members and their families by recognizing the skeletal myopathy may prevent some premature sudden deaths secondary to cardiac conduction disturbances.

Methods

We studied the index patient with a complete clinical examination, serum enzymes, color vision determination, ECG, chest roentgenogram, electromyography, nerve conduction studies, muscle biopsy for light and electron microscopy, resting surface and intracardiac ECG, rapid atrial pacing and treadmill stress test. Field visits were made to examine another 19 members of the family. Special studies obtained in these patients included serum enzymes, ECG, chest roentgenograms and determination of color vision. All available medical records of family members were collected. Four affected males and three carrier females were examined and detailed documentation was available for one more affected male who had died previously.

Case Studies

Our index patient was a 31-year-old hardware delivery man who was referred because of general weakness of 3 weeks duration and a slow pulse. The patient had been in good general health all his life and had done more than 8 years of military duty without difficulty, leaving service at age 28 years. He had, however, noticed that his arms were always small and he had a peculiar gait, his pulse was slow and he was unable to lift heavy objects by bending over, although by kneeling down he could handle up to 100-lb loads.

Cardiac examination showed a heart rate of 35 beats/min, regular rhythm, and no cardiac enlargement, gallop or murmur. Neurologic examination showed normal intelligence, a lordotic stance and gait, slight flattening of facial features and marked symmetrical atrophy of biceps and triceps with relative sparing of deltoids. There was moderate involvement of the other muscles in the shoulder girdle, the paraspinal muscles, the glutei and the tibialis anterior. Tendon jerks were absent in the arms and reduced in the ankles; sensory and cerebellar functions were normal. There were very mild contractures of the biceps and Achilles tendons. Atrophy of humeral muscles, however, was the most striking feature of neurologic examination (fig. 1).

Creatine phosphokinase was mildly increased but transaminase and lactic dehydrogenase were normal. Heart size was borderline on chest x-ray. Resting ECGs showed marked sinus bradycardia, varying from 33-48 beats/min. Conduction varied from first-degree atrioventricular block with a markedly prolonged PR interval to Wenckebach phenomenon, and then to complete atrioventricular dissociation with a slow junctional escape rhythm. QRS also showed a left anterior hemiblock pattern (fig. 2). Abnormal sinus node function was further shown by complete suppression of the sinus node after atrial pacing at rates as low as 64 beats/min. Intravenous injection of atropine 1 mg accelerated the sinus rate to 70 beats/min with a 1:1 ventricular capture, although the PR interval remained markedly prolonged (0.62 second). Exercise tolerance was normal with a maximal heart rate of 145 beats/min. The echocardiogram showed borderline abnormality of left ventricle, with mild dilatation of the cavity, relatively thin walls and slightly diminished contractility (fig. 3). A permanent cardiac pacemaker was implanted and resulted in immediate improvement in general strength. Further neurologic studies showed a nor-
normal nerve conduction time and an electromyogram suggestive of neurogenic myopathy. Muscle biopsy findings were typical of a primary myopathy, i.e., random distribution of atrophic muscle fibers, splitting within the fibers and central migration of sarcolemmal nuclei.

We have obtained information about 101 family members. Twelve male members were found to have various degrees of involvement with the same process and six had needed a pacemaker. The pedigree (fig. 4) shows that the transmission of this disease occurs in an x-linked pattern. Females are not involved, but

**Figure 1.** Frontal view and profile of the index patient with inset showing left arm. The characteristic body habitus and distribution of muscular dystrophy, especially the marked atrophy of humeral muscles and mild biceps contractures, are illustrated.

**Figure 2.** Twelve-lead resting surface ECG and rhythm strip of atrial electrogram (AE) of index patient showing sinus rate of 48 beats/min, atrioventricular dissociation and a junctional escape rhythm at a rate of 34 beats/min.

**Figure 3.** Echocardiogram of index patient. IVS = interventricular septum; LVPW = left ventricular posterior wall; ΔLVD = systolic change in left ventricular dimension.
transmit the disease to approximately one-half of their male children. A summary of the salient clinical features of 12 affected males is shown in figure 5. Two other case histories are illustrative and typical.

**Patient IV-6**

The proband’s eldest brother had a similar gait and stance with small arm muscles and also had flexion contractures at his elbows. He had mild cardiomegaly.

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**Figure 4.** Pedigree of the family with x-linked muscular dystrophy. Family branches not showing the disease are not shown.

**Figure 5.** Clinical data in 12 affected male members of the family.
with a grade IV systolic ejection murmur in the pulmonic area. The patient developed a complete atrioventricular block at age 29 years for which a permanent pacemaker was implanted. Three years later he died suddenly, perhaps as a result of pacemaker failure.

Patient IV-14

A maternal cousin of the index patient had normal milestones in infancy but at age 3 years he was found to have small muscles in his arms. At 8 years, he had lumbar lordosis and flexion contractures at the elbows. A muscle biopsy showed myopathic features. At 22 years his heart was enlarged and there was a grade III systolic murmur over the precordium. An ECG showed atrial flutter with complete atrioventricular block and a junctional escape rhythm with right bundle branch block. A permanent pacemaker was implanted.

Discussion

Progressive muscular dystrophy of Duchenne’s is a familiar x-linked trait in which cardiomyopathy, cardiomegaly and congestive heart failure occur in a majority of cases. The ECG shows a characteristic abnormality of initial depolarization seen as tall R waves in lead V1 and Q waves in inferolateral leads.1, 2 Recently a similar but less common and more benign form of muscular dystrophy was described by Becker in which cardiomyopathy is rare and the ECG changes of Duchenne’s are absent.3-5 Four other reports of families similar to ours have appeared, but all have almost identical clinical features and constitute a third distinct form of x-linked muscular dystrophy. The first description was by Dreifuss and Hogan in 1961 and was called an “unusual type of benign x-linked muscular dystrophy.”6 Subsequently it has been called x-linked scapuloperoneal syndrome by Thomas et al.,7 scapulo-humero-distal muscular dystrophy with contractures and arrhythmias by Rotthauwe et al.8 and humeroperoneal neuromuscular disease by Waters et al.9 Although all families showed evidence of similar cardiac disease, the preeminence of cardiac involvement was not emphasized in the initial reports.

In the family of Dreifuss and Hogan (later described further by Emery and Dreifuss and by McKusick), there were 11 affected males.6, 10, 11 Four young patients, ages 24 years or younger, showed no cardiac abnormality. Three had systolic murmurs, one had severe heart failure and five had various arrhythmias including atrial fibrillation, atrial flutter, atrial standstill and slow nodal rhythms. One patient died of a fatal heart attack at age 46 years.

The family described by Thomas et al.7 had six affected males. All the older patients who underwent cardiac examination had systolic murmurs and ECG abnormalities including atrial fibrillation, variable PR interval and slow junctional rhythm with intraventricular conduction defect. Two of their patients had markedly enlarged hearts and died suddenly. One had an autopsy which showed dilated ventricular chambers and fibrous replacement of the myocardium.

Rotthauwe et al. described 17 males in three generations of a Bavarian family who had an x-linked muscular dystrophy in which contractures were particularly marked and included the paraspinal muscles.9 Nine of their patients died suddenly between the ages of 37-49 years. Two of them were known to have atrial paralysis, slow junctional rhythm and premature ventricular depolarizations before their death. One more patient, age 41 years, had the same rhythm disturbances. One patient in his mid-40s developed atrial flutter with slow ventricular response and premature ventricular depolarizations. Three other patients developed atrial tachycardia with second- or third-degree atrioventricular block between ages 16-24 years. Younger patients had either normal ECGs or slight prolongation of PR interval and atrial premature depolarizations.

Waters et al. reported two families with 37 affected males.8 Fifteen afflicted patients died before age 50 years after having bradycardia and syncope. All of the 15 patients who had ECGs showed atrial arrhythmias or atrial paralysis and several had partial or complete atrioventricular block with bradycardia. His bundle electrograms in three patients showed prolonged HV time. All eight patients with bradycardia had third heart sounds and systolic ejection murmurs along left sternal border. Although echocardiograms in the bradycardia patients showed dilated, hypertrophied ventricles, there was no overt failure.

The type of muscular dystrophy represented by these families is probably rare, but may be overlooked because the myopathic changes are subtle and have not been widely recognized as a separate entity. For example, this syndrome is not included in recent review of cardiomyopathies.1, 12, 13 If an otherwise healthy male has atrophic arms or contractures of the biceps or Achilles tendons, this syndrome should be suspected. In young men who develop atrioventricular block, these telltale signs should be looked for, and careful family histories obtained so that appropriate genetic counselling can be given, particularly to carrier females.

The essential distinguishing features of this syndrome from the other two types of x-linked muscular dystrophies are that the myopathy is slowly progressive and may be very subtle; it is most marked in the humeral muscles instead of pelvicofemoral muscles as in the other two types. There is a particular predilection for contractures but pseudohypertrophy is absent. Systolic ejection murmurs are frequently heard, as in Duchenne’s. But the abnormality of initial depolarization characteristic of Duchenne’s is absent. Even more important, cardiomyopathy is more frequent and manifests primarily as disturbance of impulse generation, impaired conduction and sudden death, which may be prevented by pacemaker implantation.
Dual Atrioventricular Nodal Pathways: A Common Electrophysiologic Response in Children

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SUMMARY Electrophysiologic investigation was performed on 61 children and young adults during evaluation of either cardiac dysrhythmia or pre- or postoperative congenital heart disease. The results of these studies were reviewed retrospectively to determine if longitudinal dissociation of the atrioventricular node (AVN) was present. Dual AVN pathways were detected by the atrial extrastimulus technique, using His bundle electrograms. A discontinuous $H_2H_4$ response curve indicated the presence of dual AVN pathways. There was a higher incidence of dual AVN pathways in patients with clinically evident paroxysmal supraventricular tachycardia (PSVT) than in those without PSVT. Dual AVN pathways were equally prevalent in children with corrected and uncorrected congenital cardiac defects.

FUNCTIONAL longitudinal dissociation of the atrioventricular node (AVN) has been well documented in both animals and human adults. The presence of these fast and slow conduction pathways has been shown frequently in adults with paroxysmal supraventricular tachycardias (PSVT), in which the slow pathway conduction is usually antegrade and the fast pathway conduction retrograde, thus establishing the reentry circuit for PSVT. This is a separate group from those with extranodal accessory connections, which are also found commonly in patients with PSVT. Dual AVN pathways have been found in asymptomatic adults who have undergone electrophysiologic studies. In one series, 10% of the adults undergoing electrophysiologic studies had dual AVN pathways. Although the presence of dual AVN pathways was documented using His bundle electrograms for the first time in a child, there have been no studies to determine the frequency with which dual AVN pathways occur in children with or without congenital cardiac defects or PSVT. Therefore, we analyzed the records of children studied electrophysiologically in our laboratory to determine the frequency of occurrence of dual AVN pathways in subjects with an anatomically normal heart, with or without PSVT, and those with a congenital cardiac defect, both before and after surgery.

Materials and Methods

The records of all 61 children and young adults who had atrial extrastimulus studies in our laboratory between January 1976 and December 1977 were analyzed. These children were not included in our

References


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