Cardiac involvement in congenital myotonic dystrophy

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Abstract

Seven young patients (mean age 19 years 8 months) with congenital myotonic dystrophy and with defined symptoms at birth were investigated by electrocardiography and echocardiography. None had cardiovascular symptoms. Electrocardiograms or echocardiograms or both were abnormal in all patients. Atrioventricular and intraventricular conduction defects were the most common electrocardiographic abnormalities and were seen in five patients. The echocardiographic examinations showed impaired left ventricular systolic function in one patient. Other echocardiographic findings were a small left ventricle and atrium, minor valve defects, and mitral valve prolapse.

This study shows that the heart is often affected in young patients with congenital myotonic dystrophy. The specialised conduction system is often affected and so too is the myocardium, causing impaired systolic function.

Myotonic dystrophy is a multisystem disease that is inherited in an autosomal dominant fashion at a locus on chromosome 19.[1] The disease is characterised by variable expression and severity, and symptoms usually appear when the patient is between 20 and 50 years old.[2] In adults the heart is often affected,[3] and the high incidence of sudden unexpected death, probably owing to arrhythmias or high degree atrioventricular block, is a major unsolved clinical problem in this disease.[4,5] Electrocardiographic and echocardiographic studies showed that the heart disease is progressive and that its severity corresponds to the severity of the neuromuscular disability.[6-8]

The term congenital myotonic dystrophy is applied to a subgroup of patients who have severe symptoms at birth. Newborn patients have respiratory and feeding problems, muscular hypotonia, and arthrogryphosis.[9] Neonatal mortality is high. In surviving children a severe form of myotonic dystrophy develops with both neuromuscular and intellectual disability.[10] The genetic defect in congenital myotonic dystrophy is inherited via the mother and the possibility of non-mendelian cytoplasmic transmission was suggested.[11,12]

We used electrocardiography and echocardiography to assess the extent to which the heart was affected in young patients with congenital myotonic dystrophy.

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Patients and methods

We studied seven young patients with congenital myotonic dystrophy who fulfilled the diagnostic criteria of Volpe during the newborn period.[9] Table 1 shows some of the neonatal features in the patients. We studied all surviving patients with congenital myotonic dystrophy who had been diagnosed since 1970 at the Department of Paediatrics, Central Hospital, Boden, Sweden. This department serves the coastal region of Norrbotten, the northernmost province of Sweden, with 95 000 inhabitants and an exceptionally high prevalence of myotonic dystrophy.[7] The mean age of the patients was 19·7 years (range 11–27 years). Table 1 presents some additional clinical characteristics of the patients. There were two pairs of siblings (patients 2 and 3 and 6 and 7). Most patients were thinner than normal, and only one had a body mass index of >20 kg/m^2. Six patients had a straight or scoliotic thoracic spine and a short anteroposterior thoracic diameter.

The severity of the neuromuscular disability was classified on the basis of the patient's ability to perform those daily activities that can be limited by neuromuscular symptoms: *mild*, subjective symptoms but no functional disturbances; *moderate*, functional disturbances but the patient is able to undertake all activities of daily life and is able to do a light job; *severe*, major functional disturbances with the patient being incapable of undertaking most daily activities. Intellectual disability was classified according to the patient's ability to read ordinary texts: *mild*, minor reading difficulties; *moderate*, pronounced reading difficulties; *severe*, the patient was unable to read. The severity of neuromuscular disability was classified as mild in one, moderate in five, and severe in one of the patients; and the intellectual disability was classified as moderate in three and severe in four of the patients. None of the patients had any symptoms attributable to heart dysfunction or was taking medication known to induce electrocardiographic or echocardiographic changes. All patients had a normal blood pressure.

A 12 lead electrocardiogram (I, II, III, aVR, aVL, aVF, V1–V6) was recorded at a paper speed of 50 mm/s. The evaluation included a classification according to the Minnesota code[13] of arrhythmias, P wave amplitude, atrioventricular and intraventricular conduction defects, Q and QS patterns, hypertrophy patterns, ST elevation/depression, and T wave features. We used the criteria of Castellanos and Lemberg for fascicular blocks.[14] A P wave

Table 1 Clinical characteristics of seven patients with congenital myotonic dystrophy

	Patient number						
	1	2	3	4	5	6	7
Sex	F	F	M	F	F	F	M
Age (yr)	26	27	25	11	19	16	14
BMI (kg/m²)	14·4	15·6	16·5	15·2	18·7	21·2	14·8
Severity of disease	Mod	Mod	Mod	Mild	Mod	Mod	S
Intellectual deficit	Mod	S	S	Mod	Mod	S	S
Maternal heredity	+	+	+	+	+	+	+
Neonatal features:							
Breathing problems	+	*	+	+	+	+	–
Feeding problems	*	+	+	+	+	+	+
Hypotonia	+	+	+	+	+	+	+
Facial diplegia	*	+	+	*	*	*	+
Arthrogryphosis	+	+	+	+	+	+	+
Thoracic deformity	+	+	+	–	+	+	+

BMI, body mass index, Mod, moderate; S, severe; *data not available.

of >0·13 mm was defined as broadened. The QT interval was corrected for differences in heart rate by a modification of Bazett's formula ($QTc = QT/\sqrt{RR}$, where the QTc interval is the corrected value of the QT interval and RR is the cardiac cycle length.[15]

An ATL Ultramark 8 sonograph (Advanced Technology Laboratories, Bothell, Washington, USA) was used for M mode, cross sectional, and Doppler echocardiography. The patients were examined lying on their left side and back while breathing quietly, and traces were obtained with the transducers in the parasternal, apical, and subcostal positions. M mode measurements were performed in accordance with the standards of the American Society of Echocardiography,[16] and the values obtained were compared with normal values presented by Henry *et al.*[17] Left ventricular systolic function was measured as fractional shortening (left ventricular end diastolic diameter minus left ventricular end systolic diameter divided by left ventricular end diastolic diameter). Right ventricular dimensions and systolic function were subjectively estimated as normal or abnormal. Mitral valve prolapse was diagnosed when the criteria of Devereux *et al*[18] were fulfilled. We defined hyperrefractile myocardial echoes as strongly refractile myocardial echoes persisting in different projections or angulations at gain settings low enough to eliminate completely the echoes from the surrounding endocardium and myocardium.[19]

Table 2 Electrocardiographic findings in seven patients with congenital myotonic dystrophy

	Patient number						
	1	2	3	4	5	6	7
Sinus rhythm	+	+	+	+	+	+	+
Extrasystoles	–	–	–	–	–	+	–
Heart rate (beats/min)	86	57	68	94	77	77	78
P wave	N	N	N	N	N	N	N
First degree AV block	+	+	+	–	–	+	+
PQ interval (s)	0·20	0·22	0·24	0·16	0·18	0·20	0·21
IV block	LBBB	LAFB	LAFB	–	LAFB	–	LPFB
QRS interval	0·13	0·11	0·10	0·08	0·08	0·09	0·09
QT interval (s)	0·37	0·42	0·40	0·30	0·34	0·39	0·37
QTc interval (s)	0·44	0·41	0·43	0·38	0·38	0·44	0·42
T wave	N	N	N	N	N	N	N
QRS axis (degrees)	±0	−40	−45	+90	−40	+80	+135
ST deviation	–	–	–	–	–	–	–

N, normal; AV, atrioventricular; IV, intraventricular; LBBB, left bundle branch block; LAFB, left anterior fascicular block; LPFB, left posterior fascicular block.

Table 3 Echocardiographic findings in seven patients with congenital myotonic dystrophy (abnormal results are underlined)

	Patient number						
	1	2	3	4	5	6	7
Aortic diameter (mm)	25	22	24	18	22	20	19
Left atrial diameter (mm)	28	28	27	30	29	21	27
LVD(D) (mm)	40	40	38	33	32	41	39
LVD(S) (mm)	28	28	22	23	21	28	29
IVS (mm)	8	10	11	7	8	9	9
PWT (mm)	8	9	11	7	8	10	8
Fractional shortening (%)	30	30	42	30	34	32	26
Normal right ventricle	+	+	+	+	+	+	+
Valve abnormality	MR	MVP	TR	–	–	–	–
Hyperrefractile myocardial echoes	–	–	–	–	–	–	–

LVD(D), left ventricular end diastolic diameter; LVD(S), left ventricular systolic diameter; IVS, interventricular septal thickness; PWT, left ventricular posterior wall thickness; MR, mitral regurgitation; TR, tricuspid regurgitation; MVP, mitral valve prolapse.

Results

Table 2 shows the electrocardiographic findings. Six patients had abnormal electrocardiograms with atrioventricular or intraventricular conduction defects or both. First degree atrioventricular block was found in five, left anterior fascicular block in three, left bundle branch block in one, and left posterior fascicular block in one of the patients. There were combined atrioventricular and intraventricular conduction defects in four electrocardiograms. All patients had normal sinus rhythm; one had solitary supraventricular extrasystoles. Hypertrophy patterns, abnormal Q waves, prolonged QT intervals, or ST-T changes were not found.

Table 3 shows the echocardiographic findings. The echocardiograms were abnormal in all patients. The left ventricular end diastolic diameter was shorter than normal in three patients, and two of these also had a short left ventricular end systolic diameter. One of the patients showed decreased fractional shortening with normal left ventricular dimensions and no local hypokinesia. One echocardiogram fulfilled the criteria of mitral valve prolapse. Doppler echocardiography showed mitral regurgitation in one and tricuspid regurgitation in another of the patients. These regurgitations were minor, but in both cases sufficiently large to be classified as abnormal by the investigator. The patients with mitral valve abnormalities had normal left ventricular dimensions and fractional shortening, and the patient with tricuspid regurgitation had no signs of right ventricular abnormalities. None of the patients had wall hypertrophy, ventricular dilatation, pericardial effusions, or abnormal myocardial texture.

Discussion

Congenital myotonic dystrophy is a rare disorder. O'Brien and Harper estimated the prevalence as 1 per 100 000 inhabitants in Wales,[20] and Wesström *et al* reported an incidence of 1 per 3350 live births in Sweden.[21] Our seven patients live in a region with 95 000 inhabitants and an exceptionally high prevalence of myotonic dystrophy.[7] A high regional prevalence is a prerequisite of systematic studies; this may explain why the effect of congenital myotonic dystrophy on the heart has not been studied before. The absence of young children in our series is probably the result of genetic counselling during the past decades.

Our knowledge of the prevalence and features of the heart disease associated with myotonic dystrophy is based on electrocardiographic and echocardiographic studies of patients in whom symptoms generally started in adulthood. Occasional patients with congenital disease are probably included in these series, but usually these cannot be identified from patient data. Electrocardiographic abnormalities were reported in most patients with myotonic dystrophy.[3] We found, in a recent study, abnormal electrocardiograms in 63% of all patients and in 96% of those with severe neuromuscular disability.[7] Atrioventricular and intraventricular conduction defects were the most common abnormalities but atrial fibrillation, abnormal Q waves, and repolarisation abnormalities were found in patients with severe neuromuscular disability. Echocardiographic and radionuclide studies have shown that the myocardium is affected in some patients with myotonic dystrophy, causing ventricular wall hypertrophy, left ventricular dilatation, and reduced fractional shortening.[3 7 22] In another echocardiographic study of another 30 adult patients we found left ventricular dilatation in six (20%), decreased left ventricular systolic function in five (17%), and left ventricular hypertrophy in four (13%).[8] The frequency and severity of electrocardiographic and echocardiographic abnormalities increased with the increasing severity of neuromuscular disability.[7 8]

In this study we found electrocardiographic abnormalities in six out of seven patients with congenital myotonic dystrophy. The main electrocardiographic finding, a high prevalence of atrioventricular and intraventricular conduction defects, accords with previous findings in patients with onset of symptoms in adulthood. No electrocardiogram in this series showed atrial fibrillation, abnormal Q waves, or repolarisation abnormalities—all signs of myotonic dystrophy that occur in adults with severe myotonic dystrophy.[7] We found echocardiographic abnormalities in all seven patients. Myocardial involvement with decreased left ventricular systolic function was, however, found in only one of the patients. No echocardiogram showed left ventricular hypertrophy or left ventricular dilatation. The clinical significance of some of these echocardiographic changes such as subnormal left ventricular and atrial dimensions and minor valve regurgitation without other signs of heart dysfunction is unclear. Subnormal body mass indices and thoracic deformities may have contributed to these findings. Several groups have reported an increased prevalence of mitral valve prolapse in patients with myotonic dystrophy,[23 24] but we did not find any clear overrepresentation of this anomaly in our study. A putative causal association between myotonic dystrophy and mitral valve prolapse was also questioned because myxomatous degeneration of the mitral valve or localised myocardial dysfunction have not been reported in myotonic dystrophy.[5 25]

We found signs of electrocardiographic or echocardiographic signs of heart involvement in all the patients with congenital myotonic dystrophy that we examined. Conduction defects were the main electrocardiographic finding. There were signs of impaired left ventricular function in one of the patients. The course and clinical implications of these features remain to be investigated.

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