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Electrocardiographic findings in myotonic dystrophy

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SUMMARY Sixty five patients with myotonic dystrophy, from a defined population in northern Sweden with an extremely high prevalence of this disease, were examined by electrocardiography. The patients were subdivided into three groups according to the severity of the disease. Abnormal electrocardiograms were found in 6 (35%) patients with mild disease, 12 (50%) patients with moderate disease, and 23 (96%) patients with severe disease. First degree atrioventricular block and left anterior hemiblock were the most commonly encountered abnormalities in patients with mild and moderate disease, whereas atrial fibrillation and flutter, abnormal Q waves, and repolarisation abnormalities were more common in patients with severe disease.

This study shows that the heart is often affected by myotonic dystrophy. These effects can be detected by electrocardiography in early and mild forms of the disease. The effect on the heart is progressive and clinically important atrial arrhythmias and electrocardiographic abnormalities which are useful in differential diagnosis are common in severe forms of the disease.

Myotonic dystrophy is a multisystemic disease which is inherited in an autosomal dominant fashion at a locus on chromosome 19.[1] Myotonia and devastating muscle atrophy are characteristic features, but other organ systems may also be affected and the clinical presentation is variable. Some individuals manifest the full range of skeletal, cardiac, and smooth muscle abnormalities as well as skeletal changes, cataracts, endocrine dysfunction, and mental retardation. Others have only cataracts or an individual symptom complex such as heart disease or dysphagia.[2] Experimental and clinical data suggest that myotonic dystrophy represents a genetically induced primary alteration in the structure and function of cellular membranes, but the specific metabolic defect has not been defined.[3] It has recently been proposed that myotonic dystrophy may represent not one isolated entity but a class of genetic defects having a similar clinical expression.[4]

There is electrocardiographic evidence of heart disease in most patients with myotonic dystrophy.[5] Although abnormalities do not produce symptoms in most patients, some show severe symptoms as a result of conduction and rhythm abnormalities. Thus well documented cases of complete atrioventricular block and malignant ventricular arrhythmias have been reported.[6 7] Echocardiographic and radionuclide angiocardiographic studies have shown impaired left ventricular function[8 9] but symptomatic cardiac failure is an uncommon feature of the disease.[5] A high frequency of mitral valve prolapse has been reported in myotonic dystrophy[10] but the existence of a causal relation has recently been questioned.[11]

Information on the course of the heart disease and its relation to the severity of neuromuscular symptoms is still sparse,[12] and the reported frequency of various electrocardiographic abnormalities varies considerably.[5 11 13] Available data are, however, based on small series of patients in varying stages of the disease and besides, some workers have focused only on arrhythmias and conduction disturbances and less attention has been paid to signs indicating myocardial damage and repolarisation abnormalities.

We have assessed the frequency of all types of electrocardiographic alterations in patients with myotonic dystrophy. Because the prevalence of the disease was high in the population we examined, we were able to study a large number of cases.

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Patients and methods

We studied 65 consecutive patients with the diagnosis of myotonic dystrophy investigated at either the County Hospital, Boden, or the County Hospital, Luleå, Sweden, from 1980 to 1986. These two hospitals serve a region in the coastal region of Norrbotten, the northernmost county in Sweden, with 95 000 inhabitants. The diagnosis of myotonic dystrophy was based on neuromuscular investigation and confirmatory electromyography when the clinical findings were equivocal. Only patients with a positive family history, distinct myotonia, and distal muscular weakness were included. To avoid chance inclusion of patients with asymptomatic coronary artery disease and age related degenerative disease of the cardiac conduction system we excluded men aged >50 and women aged >60. None of the patients included in the study had heart disease of other causes or was on medication with drugs known to induce electrocardiographic changes.

The severity of the disease 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.

A 12 lead electrocardiogram (I, II, III, −aVR, aVL, aVF, V1–V6) with the conventional amplification (1 mV = 10 mm) was recorded at a paper speed of 50 mm/s. All electrocardiograms were evaluated independently by two clinical physiologists. If they did not agree on the interpretation a third reading was conducted together with a cardiologist. The evaluation included a classification according to the Minnesota code[14] of arrhythmias, P wave amplitude, atrioventricular and intraventricular conduction defects, Q and QS patterns, hypertrophy patterns, ST depression/elevation, and T wave features. We used the criteria of Castellanos and Lemberg for hemiblocks[15]. A broadened P wave was defined as >0·13 mm. 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 and RR is the cardiac cycle length).[16] QTc values of 0·44 s for men and 0·46 s for women were used as upper limit of normal. Q waves and repolarisation alterations were classified as abnormal or possibly abnormal. Recordings with a prolonged QT interval or a broadened P wave were classified as abnormal. The prevalence of various electrocardiographic abnormalities was compared with results in a normal population.[17] Age standardized rates[18] were calculated with the age distribution in the entire series as the standard.

Results

We studied 65 patients (33 men and 32 women). The mean age for the series was 37·2 years. Table 1 shows the distribution of patients according to the severity of the disease. There were 17 patients (26%) with mild, 24 (37%) with moderate, and 24 (37%) with severe disease. There were more men than women in the group with mild disease and more women than men in the group with severe disease. The mean age of the patients was 31·4 years in the group with mild disease, 37·4 years in the group with moderate disease, and 41·1 years in the group with severe disease.

Table 2 shows the electrocardiographic findings in the entire series of patients and in each of three patient groups with varying severity of disease. Electrocardiograms with at least one abnormal feature were found in 41 (63%) of 65 patients, while alterations classified as possibly abnormal were found in another five (8%). The proportion of recordings showing abnormalities increased with the severity of the disease and was 35% in mild disease, 50% in moderate disease, and 96% in severe disease. The remarkable features are the high frequency of abnormal electrocardiograms in the entire series of patients and the concentration of cases with atrial fibrillation and flutter, abnormal Q waves, and repolarisation abnormalities in the subset of patients with the most severe form of systemic disease. Table 3 shows the distribution according to age and severity of the disease and age standardised frequency rates of individuals with an abnormal electrocardiogram. The proportion of abnormal electrocardiograms also increased with the severity of neuromuscular symptoms after standardisation for age.

Sinus rhythm was present in all patients with mild, in 96% of patients with moderate, and in 67% of patients with severe disease. Atrial fibrillation or

Table 1 *Patients with myotonic dystrophy: distribution by age, sex, and severity of disease*

				Age (yr)	
Severity of disease	*No*	*M*	*F*	*Mean (SD)*	*Range*
Mild	17	14	3	31·4 (11·6)	17–52
Moderate	24	13	11	37·4 (13·2)	19–57
Severe	24	6	18	41·1 (11·9)	24–59
Total	65	33	32	37·2 (13·9)	17–59

Table 2 *Electrocardiographic findings in 65 patients with myotonic dystrophy*

	Severity of disease			
	Mild	*Moderate*	*Severe*	*Total*
Complete ECG evaluation:	*(n = 17)*	*(n = 24)*	*(n = 24)*	*(n = 65)*
Abnormal ECG	6 (35%)	12 (50%)	23 (96%)	41 (63%)
Suspected abnormal ECG	2 (12%)	2 (8%)	1 (4%)	5 (8%)
Rhythm:				
Sinus rhythm	17 (100%)	23 (96%)	16 (67%)	56 (86%)
Atrial fibrillation	0	0	2	2 (3%)
Atrial flutter	0	1	4	5 (8%)
Pacemaker	0	0	2	2 (3%)
AV and IV block:*	*(n = 17)*	*(n = 24)*	*(n = 22)*	*(n = 63)*
First degree AV block	3 (18%)	5 (21%)	5 (23%)	13 (21%)
LAH	2 (12%)	3 (13%)	6 (27%)	11 (18%)
LPH	0	1	0	1
RBBB	1	1	1	3
LBBB	0	2	0	3
Atypical BBB	0	1	3	4
LAH + RBBB	0	0	0	0
First degree AV block + IV block	1	3	4	8
P waves:†	*(n = 17)*	*(n = 23)*	*(n = 16)*	*(n = 56)*
Broadened P waves	0	2 (9%)	1 (6%)	3 (5%)
Q waves‡:	*(n = 16)*	*(n = 20)*	*(n = 18)*	*(n = 54)*
Abnormal	1 (6%)	5 (25%)	9 (50%)	15 (28%)
Abnormality suspected	1 (6%)	0	1 (6%)	2 (4%)
Repolarisation abnormalities:‡	*(n = 16)*	*(n = 20)*	*(n = 18)*	*(n = 54)*
ST elevation				
Abnormal	1	1	0	2 (4%)
Abnormality suspected	0	1	1	2 (4%)
ST-T depression				
Abnormal	0	1	7	8 (15%)
Abnormality suspected	0	0	0	0
Flattened T waves				
Abnormal	1	1	0	2 (4%)
Abnormality suspected	1	1	1	3 (6%)
Negative T waves				
Abnormal	0	0	5	5 (9%)
Abnormality suspected	0	0	0	0
Prolonged QT interval	0	0	3 (17%)	3 (6%)

*Those with pacemakers excluded; †those with pacemaker, atrial fibrillation, and atrial flutter excluded; ‡those with pacemaker and bundle branch block excluded.
AV, atrioventricular; IV, intraventricular; LAH, left anterior hemiblock; LPH, left posterior hemiblock; RBBB, right bundle branch block; LBBB, left bundle branch block.

flutter occurred in one (4%) of the patients with moderate and in six (25%) of the patients with severe disease. Two patients, both belonging to the subset of patients with severe disease, had had a pacemaker implanted: one because of sinus node dysfunction and symptomatic bradycardia and the other because of complete atrioventricular block and Adams-Stokes attacks.

Table 3 *Distribution of 41 patients with abnormal electrocardiograms according to age and severity of disease*

	Severity of disease			
Age group (yr)	*Mild (n = 6)*	*Moderate (n = 12)*	*Severe (n = 23)*	*Total (n = 51)*
29	2	3	3	8
30–39	2	2	6	10
40–49	2	5	2	9
50–59	0	2	12	14
Age-standardised rate	0·42	0·52	0·96	0·63

Conduction defects were found in 27 (42%) of the patients in the entire series. First degree atrioventricular block and left anterior hemiblock were the abnormalities most often encountered in patients with mild disease, and four of six recordings classified as abnormal in this group showed one of these two alterations. The frequency of first degree atrioventricular block was similar in all three groups, whereas the frequency of left anterior hemiblock, bundle branch block, and combined atrioventricular block and intraventricular conduction defects increased with the severity of the disease. Second degree atrioventricular block was not found in any of the recordings.

Abnormal Q waves and repolarisation abnormalities were sought on electrocardiograms without

pacemaker induced rhythm or bundle branch block and were classified as abnormal or possibly abnormal. There were abnormal Q waves in 15 (28%) of 54 recordings and another two showed Q waves that were possibly abnormal. The site of the abnormal Q waves was anterior in nine cases, inferior in five, and lateral in one. The occurrence of abnormal Q waves increased with the severity of the disease: it was 6% in mild, 25% in moderate, and 50% in severe disease.

Abnormalities of repolarisation, such as ST elevation, ST-T depression, flattened T waves, and negative T waves, were found in 17 (32%) of 54 individuals, while another four (6%) showed alterations suggestive of such an abnormality. ST-T changes were most common in patients with severe disease. A prolonged QT interval was found in three patients; all had severe disease.

A pattern typical of right or left ventricular hypertrophy was not found in any of the recordings, and a broadened P wave was found in three. Five patients had solitary supraventricular and ventricular extrasystoles.

Discussion

Although cardiac abnormalities have been recognised for many years in patients with myotonic dystrophy the pathogenesis remains unknown.[2] Histopathological studies of the heart are limited and the reported non-specific findings vary from normal structure to atrophy of myocardial muscle, diffuse myocardial fibrosis, fatty infiltration, and focal myocarditis.[19-21] The course of heart disease in myotonic dystrophy has been studied in only a limited number of patients,[12] and no close correlation between the presence of cardiac abnormalities and the severity of the systemic disease has been reported. In several cases cardiac abnormalities were reported before any other manifestation of the disease developed.[13]

Only a few patients with myotonic dystrophy are reported to have cardiac symptoms, and our findings accord with those of others. In Church's review of published cases 16% of 317 patients had cardiac symptoms, which were attributable to arrhythmias in half the cases.[5] Patients with myotonic dystrophy, however, have a higher frequency of sudden unexpected death than the general population; it has been suggested that this is owing to malignant arrhythmias or high grade conduction defects.[2]

Previous studies also show that electrocardiographic alterations are common in myotonic dystrophy, but reported figures on the frequency of abnormal electrocardiograms in patients with this disease range from 45 to 85%.[5 22] These figures are based on single cases, small scale studies, and a few series on 20–30 patients[11 13 23] To date the most comprehensive review of the subject was Church's report of electrocardiographic changes in 14 of his own cases and 222 cases from 48 published reports in which 85% of the cases showed electrocardiographic abnormalities.[5] Such reviews may be biased towards the inclusion of abnormal cases and may overestimate the frequency of electrocardiographic abnormalities. Direct comparisons of frequency figures between various studies are difficult because different criteria may have been used to classify electrocardiographic changes and because patients in varying stages of the disease will have been included. Also some workers have focused on arrhythmias and conduction abnormalities only, and less attention has been paid to QRS configuration and changes in repolarisation. The commonest electrocardiographic abnormality in several reports is first degree atrioventricular block followed by various types of intraventricular conduction defects and atrial arrhythmias, in particular atrial fibrillation and flutter.

In the present study patients with myotonic dystrophy were classified according to the severity of the disease and the frequency of abnormal electrocardiograms correlated with the severity of the disease. Mean age increased with the severity of the disease and this may be a confounding variable, despite the upper age limits of the group that we studied. Nevertheless, age standardised frequency rates also correlated with disease severity, which strongly indicates that the cardiac disease in myotonic dystrophy is progressive.

Suggested causes of sudden unexpected death in myotonic dystrophy, in which the frequency of first degree atrioventricular block and bundle branch block is so high, are conduction defects progressing to complete atrioventricular block and terminating in asystole or ventricular fibrillation. A serial electrophysiological study has shown a progressive dysfunction of the His-Purkinje system,[11] but there are only a limited number of cases with complete atrioventricular block in published reports.[6] Our findings of an increasing frequency of intraventricular conduction defects as disease severity and age of the patients increases support the hypothesis that the conduction disturbances are progressive. Conduction abnormalities are not common in other myotonic disorders, and thus the finding of conduction abnormalities may be of additional diagnostic value in myotonic dystrophy.

Dysfunction of the sinus node was the underlying abnormality in one of our patients who had required the implantation of a pacemaker. Although bradycardia was the first sign of cardiac dysfunction

to be described in a patient with myotonic dystrophy,[24] there are few reported cases of symptomatic sinus node dysfunction.[25 26] Five of twenty patients with normal heart rate who had an electrophysiological investigation had an abnormal sinus node recovery time.[23] There are too few histopathological studies of sinus node tissue to permit conclusions.

Abnormal Q waves without concomitant coronary artery disease or myocardial infarction are well known electrocardiographic findings in several neuromuscular disorders such as Duchenne muscular dystrophy and Friedreich's ataxia. Pseudoinfarction patterns in myotonic dystrophy have previously been reported in only a few cases. Abnormal Q waves were present in four of 27 cases reported by Viitasalo *et al*[23] and in five of 25 cases reported by Perloff *et al.*[11] In our study the Minnesota code was used to classify alterations in QRS configuration and recordings showing pacemaker induced rhythm and bundle branch block were excluded from this analysis. We found definitely abnormal Q waves in 28% of the patients in the entire series and suspected abnormal Q waves in another 4%. In those with the most severe disease an abnormal Q wave was present in 50% of the recordings and this was the most common electrocardiographic abnormality. We believe that myotonic dystrophy should be added to the list of metabolic and neuromuscular disorders in which Q waves are abnormal. The consequences of failure to recognise such a possibility may be serious.

We found ST-T alterations, classified according to the Minnesota code into abnormal changes or changes suspected of being abnormal, in 17 (32%) and four (7%) patients respectively, after the exclusion of recordings showing pacemaker rhythm and bundle branch block. Also these electrocardiographic changes seemed to be associated with severe neuromuscular symptoms, and were found only occasionally in patients with mild or moderate disease. There is little information in published reports about ST-T changes in myotonic dystrophy, and our findings suggest that a low frequency should be expected in series of patients in which most have mild or moderate disease. In Church's review ST-T changes were found in 42 of 236 patients, but the type of changes or the grounds for classification were not stated.[5] In the series presented by Perloff *et al*[11] and Viitasalo *et al*[23] ST-T changes were not reported. The QT interval was prolonged in three cases in our study; all had severe symptoms. The QT interval in myotonic dystrophy was analysed by Viitasalo *et al.*[23] They found a higher frequency (33%), of prolonged QT interval than we did. The clinical importance of a prolonged QT interval lies in its association with malignant ventricular arrhythmias, and the occurrence of this electrocardiographic alteration may be of prognostic importance in patients with myotonic dystrophy.

Atrial fibrillation or flutter was found in 10–21% of patients with myotonic dystrophy.[5 11] We found these arrhythmias in 11% of the entire series and in 25% of those with severe neuromuscular symptoms.

Extrasystoles were seen occasionally in five recordings in the present series, but a study like this, based on short recordings of resting electrocardiograms, will give little information about the true frequency of extrasystoles and intermittent arrhythmias.

The mechanisms by which electrocardiographic changes are brought about in patients with myotonic dystrophy are unknown and remain speculative. We believe that progressive, genetically induced, alterations in the structure and function of cellular membranes in myocardium, the specialised conduction system, and the autonomic nerves may prove to be of primary importance.

Myotonic dystrophy has often been described as a rare disease: reported prevalence ranges from 2·4 to 5·5 per 100 000 inhabitants.[1] The fact that as many as 65 patients could be included in the present study indicates a prevalence of at least 70 per 100 000 in this region in Northern Sweden. Such a high prevalence of myotonic dystrophy has, to our knowledge, not been reported before. An epidemiological study of myotonic dystrophy including the population in the two northernmost counties in Sweden has started in our hospitals.

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