JACC Vol. 11, No. 3
March 1988:662–71

MORPHOLOGIC STUDIES

Pathology of the Cardiac Conduction System in Myotonic Dystrophy: A Study of 12 Cases

HAROLD H. NGUYEN, MD, JAMES T. WOLFE III, MD,* DAVID R. HOLMES, JR, MD, FACC, WILLIAM D. EDWARDS, MD, FACC

Rochester, Minnesota

In 12 autopsy cases of myotonic dystrophy, the most frequently observed histopathologic lesions of the cardiac conduction system were fibrosis, fatty infiltration and atrophy. Fibrosis involved the sinus node in 6 cases, atrioventricular (AV) node in 7, AV bundle in 8, bundle branches in 10 and ventricular myocardium in 11. Fatty infiltration was observed in the sinus node in two cases, AV node in two, AV bundle in six, bundle branches in one and ventricular myocardium in nine. Atrophy was prominent in the AV bundle in five and bundle branches in eight. Lymphocytes infiltrated the conduction system in three cases and were associated with myotonic dystrophy in two and varicella myocarditis in one. Ventricular myocytes were hypertrophied in seven cases, vacuolated in three and exhibited disarray in two.

The distribution and extent of conduction system lesions tended to correspond to antemortem electrocardiographic abnormalities, including prolonged PR interval in six cases, intraventricular conduction delay in six and bundle branch block in four. Cardiac involvement by myotonic dystrophy may have contributed to sudden death in four cases.

(J Am Coll Cardiol 1988;11:662–71)

Myotonic dystrophy is characterized by myotonia, delayed muscle relaxation time, progressive muscular weakness and atrophy and characteristic electromyographic abnormalities. In addition to its neuromuscular features, the disorder is frequently accompanied by cataracts; frontal baldness; ptosis; various respiratory, gastrointestinal and cardiovascular symptoms; and a history of myotonic dystrophy involving other family members.

Cardiac dysfunction usually appears several years after the onset of neuromuscular symptoms but occasionally may be the first manifestation of the disease. Cardiac findings include conduction abnormalities with or without arrhythmias, dilated cardiomyopathy, mitral valve prolapse and sudden death (1–40). In three reviews (22,34,36) the frequency of conduction abnormalities ranged from 62 to 75%.

The most commonly observed conduction defects are a prolonged PR interval (first degree heart block) and intraventricular conduction delay (22,34,36). Sinus arrhythmia, atrial flutter, atrial fibrillation, second and third degree heart block, bundle branch block and ventricular tachycardia also have been reported. Investigations of the conduction system using either surface electrocardiograms (ECG) or invasive electrophysiologic studies have demonstrated abnormalities, often at multiple levels, in the atrioventricular (AV) node and the AV bundle and bundle branches (His-Purkinje system) (1,4,6,8–10,15,17).

Although the pathophysiologic findings of the cardiac conduction system have been described in many clinical studies of patients with myotonic dystrophy, the histopathologic findings, to our knowledge, have been reported in only five cases (3,16,21,31). With these considerations in mind, the present study of 12 autopsy cases was undertaken.

Methods

Study cases. From the medical records between 1950 and 1986 at our institution, 12 cases were identified in which the clinical diagnosis of myotonic dystrophy was established unequivocably, and in which an autopsy was performed and the heart was available from our tissue registry. Only those cases were included in which classic clinical features were described by a neurologist and in which there was either a characteristic electromyogram or a family history of myotonic dystrophy. One or more 12 lead ECGs, recorded within 2 years before death, were available in each case and were reviewed by one of us (D.R.H.).

From the Department of Pathology and the Division of Cardiovascular Diseases and Internal Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

*Present address: Mercy Hospital, Charlotte, North Carolina.

Manuscript received June 30, 1987; revised manuscript received September 30, 1987, accepted October 16, 1987.

Address for reprints: William D. Edwards, MD, Department of Pathology, Mayo Clinic, 200 First Street SW, Rochester, Minnesota 55905.

0735-1097/88/$3.50

Table 1. Clinical Features in 12 Cases of Myotonic Dystrophy

Case	Sex & Age (yr)	Duration of Disease (yr)	Family History	Electromyography	12 Lead ECG	Cause of Death*
1	F, 40 days	<1	Yes	Not done	Normal	Respiratory failure
2	M, 13	4	Yes	Not done	Normal	Sudden death†
3	M, 20	20	Yes	Diagnostic	1° AV block, intermittent 3° AV block, LHBB, bradycardia, IVCD, VT	Varicella myocarditis
4	M, 43	3	No	Diagnostic	1° AV block, ACD, IVCD	Bronchopneumonia
5	F, 46	14	Yes	Diagnostic	Sinus arrhythmia, bradycardia	Sudden death†
6	F, 48	2	No	Diagnostic	AF, tachycardia, SVT	Respiratory arrest
7	F, 48	28	Yes	Diagnostic	1° AV block, LBBB, ACD, IVCD	Sudden death
8	M, 49	29	Yes	Diagnostic	Sinus tachycardia, LAD, SVT, VT	Pulmonary embolus
9	F, 55	35	No	Diagnostic	1° AV block, RBBB, IVCD, SVT, VT, LAD	Myocardial infarction
10	M, 57	7	Yes	Diagnostic	1° AV block, IVCD, VPC, bradycardia	Pulmonary embolus
11	F, 57	9	Yes	Diagnostic	1° AV block, AF, ACD, IVCD, RBBB, LBBB, LAD, SVT	Sudden death
12	F, 65	45	Yes	Diagnostic	AF, SVT	Bronchopneumonia

*Based on clinical and autopsy findings; †death occurred within 24 h of an operative procedure.

1° = first degree; 3° = third degree; ACD = atrial conduction delay; AF = atrial fibrillation; AV = atrioventricular; ECG = electrocardiogram; F = female; IVCD = intraventricular conduction delay; LAD = left axis deviation; LBBB = left bundle branch block; M = male; RBBB = right bundle branch block; SVT = supraventricular tachycardia; VPC = ventricular premature complexes; VT = ventricular tachycardia.

Pathologic examination. For each cardiac specimen, the weight was recorded and the extent of ischemic and valvular disease was grossly evaluated. Tissue for study by light microscopy was obtained by one of us (W.D.E.) from the sinus node, AV conduction system, right ventricular free wall, ventricular septum and anterior, lateral and inferior aspects of the left ventricular free wall.

Tissues were processed routinely, cut 5 μm thick, and stained with hematoxylin-eosin and Masson's trichrome. From the tissue blocks of the AV conduction system, every 50th 5 μm slice was retained for study. The number of slides for each case ranged from 48 to 192 with an average of 85. Slides were reviewed without knowledge of ECG features or other clinical information.

The extent of fibrosis and fatty infiltration for the myocardium and conduction tissues was evaluated semiquantitatively and expressed as a percentage, in 5% increments, of the tissue involved. By this method, intraobserver variation was generally 0 to 5% and never >10%. Because there normally may be appreciable individual variation in the structure of the cardiac conduction system, age-matched controls were not utilized. Rather, published descriptions and photomicrographs, based on observations from a large number of cases and investigators (41–44), served as normal controls.

Results

Clinical features (Table 1). Of the 12 patients, 7 were female and 5 were male, and their ages ranged from 40 days to 65 years (mean 42 years). The duration of myotonic dystrophy ranged from 40 days to 45 years (mean 16 years). The clinical and pathologic findings in one case (Case 9) have been published previously (16).

A family history was positive in 9 cases, and an electromyogram was diagnostic in the 10 cases in which it was performed. Cataracts, frontal baldness and ptosis were present in nine cases, and ptosis alone was observed in one (Case 6); these features were absent in the two youngest patients.

Respiratory and gastrointestinal disorders were also present and included aspiration pneumonia in six cases, dysphagia in three and irritable bowel in two. Four patients had had diabetes mellitus, and one (Case 6) had had Graves' disease with thyrotoxicosis.

Cardiac symptoms included palpitation in five cases (Cases 5, 6, 9, 10 and 11), dizziness or syncope in two (Cases 5 and 9) and dyspnea in two (Cases 4 and 6). Numerous ECG abnormalities were documented (Table 1). In only one case (Case 3) were cardiac catheterization and electrophysiologic study done.

Table 2. Cardiac Pathologic Features in 12 Cases of Myotonic Dystrophy

Case	Heart Weight (g)		Hypertrophy	Dilation	Sinus Node	AV Node	Penetrating AV Bundle
	Observed	Expected*					
1	24	25	None	None	Normal	Normal	Normal
2	235	210	None	None	Fibrosis (70%)	Fibrosis (40%)	Normal
3	560	340	LV, RV	Four chamber	Fibrosis (60%)	Fibrosis (20%), lymphocytes	Normal
4	275	295	None	None	Fibrosis (60%), perinodal fibrosis	Fibrosis (30%)	Fat (50%)
5	250	265	None	None	Normal	Normal	Normal
6	315	260	LV	None	Fibrosis (60%)	Normal	Fat (40%)
7	480	280	LV, RV	Four chamber	Lymphocytes	Fibrosis (15%)	Lymphocytes
8	310	315	None	None	Fat (10%), lymphocytes	Fibrosis (40%)	Fibrosis (25%), fat (25%), lymphocytes
9	450	260	LV	None	Normal	Small	Normal
10	545	360	LV, RV	LA, RA	Fibrosis (80%), perinodal fibrosis	Fibrosis (30%), fat (30%)	Fat (50%)
11	420	270	LV, RV	Four chamber	Fibrosis (80%), fat (10%), perinodal fibrosis	Fibrosis (30%)	Atrophy
12	395	280	LV	None	Normal	Fat (40%)	Normal

*Refer to Ludwig J. Current Methods of Autopsy Practice. 2nd ed. Philadelphia: WB Saunders, 1979:668–71. AV = atrioventricular; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

Causes of death determined at autopsy included sudden death in four cases, respiratory failure in two, bronchopneumonia in two, pulmonary embolus in two, varicella myocarditis in one and ruptured acute myocardial infarction in one.

Pathologic features of myocardium (Table 2). The heart was appreciably enlarged in 6 of the 12 autopsy cases and was consistent with dilated cardiomyopathy in 3 of the 6. There was no gross evidence of a floppy mitral valve or other chronic valvular disease among the specimens, although mitral valve prolapse was detected echocardiographically in one case (Case 3).

Coronary atherosclerosis was severe (>75% obstruction of cross-sectional luminal area) in four cases and represented single vessel disease in three (Cases 4, 5 and 9) and three vessel disease in one (Case 10). No lesion of the conduction system was considered to be due to ischemia. Ischemic heart disease, however, was responsible for death in one case (Case 9) and may have contributed to sudden death in another (Case 5).

Microscopically, fibrosis involved 10 to 20% of the ventricular myocardium in the 10 adult patients (Fig. 1). The fibrosis tended to be perivascular, but pericellular and patchy replacement patterns were also encountered. Fatty infiltration was observed in the right ventricle in nine cases and in the left ventricle in three (Fig. 1).

Degenerative sarcoplasmic vacuolization of ventricular myocytes was focally present in three cases, and myofiber disarray involved the ventricular septum in two. Although cardiac hypertrophy was observed on the basis of gross heart weight in only 7 cases, myocyte nuclei were enlarged and hyperchromatic in all 12. Varicella myocarditis was diagnosed in one case (Case 3).

Pathologic features of conduction system (Table 2). *The sinus node was excessively fibrotic in 6 of the 12 cases (Fig. 2).* This finding was based on the generalization that the normal percentage of collagen in the sinus node is approximately equal to one's age in years. Fatty infiltration was present in only two cases and was mild in both. Small clusters of lymphocytes were observed along the edge of the sinus node in two cases. Myocardial tracts leaving the node were fibrotic in three cases, and dense fibrosis encased several parasympathetic ganglia near the sinus node in one (Case 10). The sinus nodal artery was normal for age in all cases.

Excessive fibrosis involved the AV node and its internodal approaches in 7 of the 12 cases (Fig. 3). For the AV conduction system, the normal percentage of collagen and fat was considered to be <10% each. Fatty infiltration of the AV node was observed in two cases, and a focal lymphocytic infiltrate in one. The AV nodal artery showed focal intimal thickening in four cases.

The penetrating AV (His) bundle was more often the site of fatty infiltration than fibrosis. It was involved by fat in four cases, fibrosis in one and small clusters of lymphocytes

Table 2. *(continued)*

Case	Branching AV Bundle	Left Bundle Branch	Right Bundle Branch	Myocardium	
				LV	RV
1	Normal	Normal	Normal	Normal	Normal
2	Fibrosis (15%)	Fibrosis (20%)	Fibrosis (20%)	Normal	Fibrosis (10%)
3	Lymphocytes	Fibrosis (20%), degeneration, lymphocytes	Lymphocytes	Fibrosis (10%), lymphocytes	Lymphocytes
4	Fibrosis (30%), fat (30%)	Fibrosis (30%), atrophy	Fibrosis (20%)	Fibrosis (15%), fat (5%)	Fibrosis (10%), fat (15%)
5	Normal	Fibrosis (40%), atrophy	Normal	Fibrosis (10%), degeneration, disarray	Fibrosis (10%) fat (15%)
6	Fat (40%), atrophy	Fibrosis (75%), atrophy	Fibrosis (20%)	Fibrosis (10%), fat (5%)	Fibrosis (10%), fat (10%),
7	Fibrosis (25%), fat (15%)	Fibrosis (60%), degeneration, atrophy	Fibrosis (35%), atrophy, lymphocytes	Fibrosis (20%)	Fibrosis (10%), fat (10%)
8	Fibrosis (35%), atrophy	Fibrosis (25%), atrophy	Not identified	Fibrosis (15%), lymphocytes	Fat (30%)
9	Fibrosis (50%), fat (20%), atrophy	Atrophy	Normal	Fibrosis (15%)	Fat (15%)
10	Fibrosis (25%), degeneration, atrophy	Degeneration, atrophy	Fibrosis (40%), degeneration, atrophy	Fibrosis (10%), degeneration	Fibrosis (10%), fat (30%)
11	Fibrosis (50%), atrophy	Fibrosis (50%), atrophy	Fibrosis (70%), atrophy	Fibrosis (15%)	Fat (10%)
12	Fibrosis (15%)	Fibrosis (20%), degeneration	Fat (30%)	Fibrosis (10%), fat (5%), degeneration, disarray	Fat (30%)

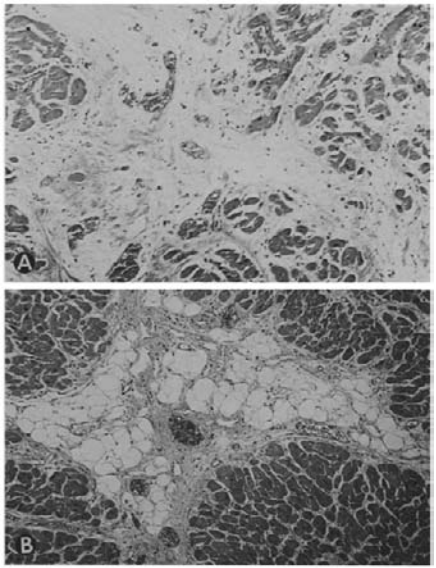

Figure 1. Case 11. Histopathology of left ventricular myocardium, without coexistent coronary artery disease, in myotonic dystrophy. **A**, Patchy replacement fibrosis and **B**, patchy fibroadipose tissue in a 57 year old woman (hematoxylin-eosin stain, original magnification ×90, reduced by 20%).

in two (Fig. 4). In contrast to the penetrating portion of the His bundle, the branching portion was more often the site of fibrosis than fatty infiltration. It was excessively fibrotic in eight cases; in five, it was also atrophic and was involved by fatty infiltration in four (Fig. 4). Lymphocytic infiltrates were encountered in one case.

The left bundle branch was fibrotic in nine cases, atrophic in eight and the site of degenerative changes in four (Fig. 5). In comparison, the right bundle branch was fibrotic in six cases, atrophic in three and degenerative in one. In one case, fat accounted for 30% of the right bundle branch. Small clusters of lymphocytes were observed in two cases.

Clinicopathologic correlations. In Case 1 (the youngest patient), both the ECG and the histologic findings in the cardiac conduction system were normal. In Case 2 (the next youngest patient), the ECG was normal, but microscopic study showed extensive fibrosis of the sinus and AV nodes and mild fibrosis of the branching AV bundle and both bundle branches. In the other 10 cases (the 10 oldest patients), abnormalities were observed in both the ECG and the microscopic study of the cardiac conduction system.

Among the 12 cases, excessive fibrosis of the sinus node was observed in 2 of 3 with atrial conduction delay, 2 of 3 with atrial fibrillation, 2 of 3 with bradycardia and only 1 of 3 with no sinus or atrial arrhythmia (Tables 1 and 2).

Excessive fibrosis of the AV node was present in five of six cases of first degree heart block but was observed in only two of six cases in which no AV conduction abnormalities were recorded.

Fatty infiltration or excessive fibrosis of the AV (His) bundle was noted in five of six cases of first degree heart block; in all six, intraventricular conduction delay was also present. Although similar lesions were also observed in four of six cases in which there were no AV conduction abnormalities, the extent was mild (15% fibrosis) in two of the four.

The left bundle branch was fibrotic in three cases of left bundle branch block and in six of nine without block. Fibrosis of the right bundle branch was observed in 1 of 2 cases of right bundle branch block and in 5 of 10 without block.

Left ventricular fibrosis (>10%) was present in three of four cases with intraventricular conduction delay and in only two of eight without it.

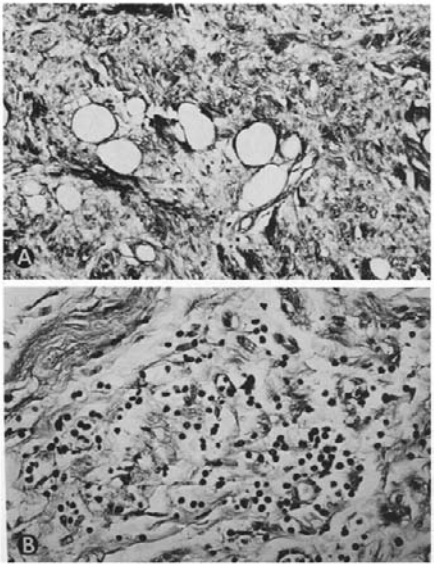

Figure 2. Histopathology of sinus node in myotonic dystrophy. **A**, Case 10. Severe fibrosis and focal fatty infiltration in a 57 year old man (Masson trichrome stain, original magnification ×180, reduced by 20%). **B**, Case 8. Lymphocytic infiltration in a 49 year old man (hematoxylin-eosin stain, original magnification ×360, reduced by 20%).

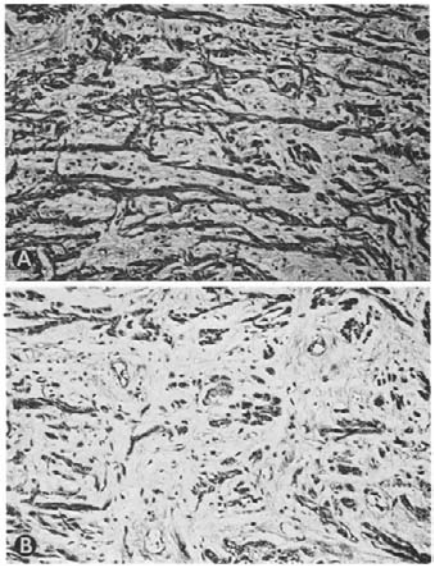

Figure 3. Histopathology of atrioventricular node in myotonic dystrophy. **A**, Fibrosis in a 13 year old boy (Case 2) and (**B**) a 49 year old man (Case 8) (Masson trichrome stain, original magnification ×180, reduced by 20%).

Discussion

Clinical features. Among patients with myotonic dystrophy, cardiac symptoms have been reported in 7 to 23% (22, 34). In the present study of 12 cases, palpitation occurred in 5 and light-headedness or syncope in 2. Four (33%) of the 12 patients had sought medical attention because of the severity of their cardiac symptoms, and all 4 had had an AV conduction defect detected on the 12 lead ECG.

Abnormalities of the cardiac conduction system are commonly observed in patients with myotonic dystrophy. The two most frequently reported findings are prolonged PR interval and intraventricular conduction delay (22,34,36). Among our 12 patients, the 10 oldest had an abnormal ECG and 6 had both a prolonged PR interval and an intraventricular conduction delay.

Pathologic features of myocardium. Although the myocardium may seem normal on light microscopy in some patients with myotonic dystrophy, it is the site of nonspecific abnormalities in most. These abnormalities have been noted in autopsy specimens in 30 reported cases and in endomyocardial biopsy specimens in 11 cases (2,3,9,11,16–19,21, 23,25–29,31,32,35,37–40).

The most frequently observed lesions include myocyte hypertrophy, with or without sarcoplasmic vacuolization or other degenerative changes, and interstitial fibrosis or fatty infiltration (2,3,9,11,12,16–18,21,23,25,26,28,29,31, 32,37–39). Even in patients with a normal heart weight, myocyte nuclei may be enlarged and hyperchromatic, as expected in hypertrophied cells. Moreover, myofiber disarray and lymphocytic infiltrates occasionally may be detected (3,11,17,19,29,31). Each of these features was observed in the present study.

In regard to ventricular function, although myocardial abnormalities are commonly observed grossly and microscopically in patients with myotonic dystrophy, and although 7% of patients have clinical evidence of heart failure (28), most echocardiographic investigations have failed to demonstrate abnormalities in ventricular function (4,6). This failure may be due to the mild nature of the pathologic abnormalities in most patients (4,13,22) or to the early stage

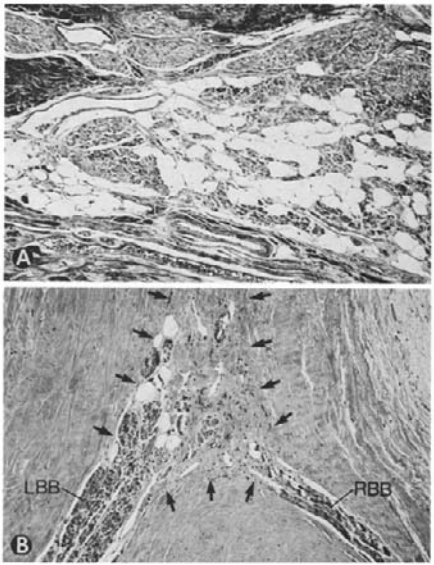

Figure 4. Histopathology of atrioventricular (AV) bundle in myotonic dystrophy **A**, Case 10. Fatty infiltration in a 57 year old man (Masson trichrome stain, original magnification ×90, reduced 20%). **B**, Case 7. Focal replacement fibrosis and atrophy in a 48 year old woman. **Arrows** demarcate expected size and shape of branching AV bundle (hematoxylin and eosin stain, original magnification ×90, reduced by 20%). LBB = left bundle branch; RBB = right bundle branch.

in the disease process at which some echocardiographic studies may have been performed (10,28).

Dilated cardiomyopathy in patients with myotonic dystrophy has been observed clinically by several authors (2,3, 25,26,31). Moreover, in a review of 23 autopsy cases, Kennel et al. (16) noted cardiomegaly in 8 (35%). In the present study, biventricular hypertrophy and four chamber dilation were noted in 3 (25%) of the 12 cases, and their presence could not be explained on the basis of ischemia or other causes. Dilated cardiomyopathy, however, was not diagnosed clinically in any of the cases.

Severe coronary atherosclerosis was observed in four cases in this study, but the location of patchy areas of ischemic fibrosis was distant from the conduction tissues and led to the conclusion that abnormalities of the cardiac conduction system in our cases were the result of myotonic dystrophy rather than ischemic heart disease. Similar observations have been made by other investigators (1,4,15,19, 22,30,36).

Pathologic features of conduction system: comparison with previously reported cases (Table 3). Detailed histopathologic investigations of the cardiac conduction system in myotonic dystrophy have been previously reported in five cases (3,16,21,31). In four cases in which abnormalities were observed, the lesions were multifocal and consisted primarily of fibrosis, fatty replacement, degenerative changes and atrophy. In the present study, the same types of lesions were documented in 11 of the 12 cases and, in general, their extent and severity tended to correlate with the extent of ECG abnormalities. Four of the 12 patients, however, were >50 years, and it is possible that aging changes may also have contributed to the observed lesions in these cases.

In some of the cases, however, histopathologic lesions existed without ECG counterparts (and vice versa), and lesions of the bundle branches had the poorest correlations. This lack of correlation may be expected because investigators using either external His bundle recordings (6) or

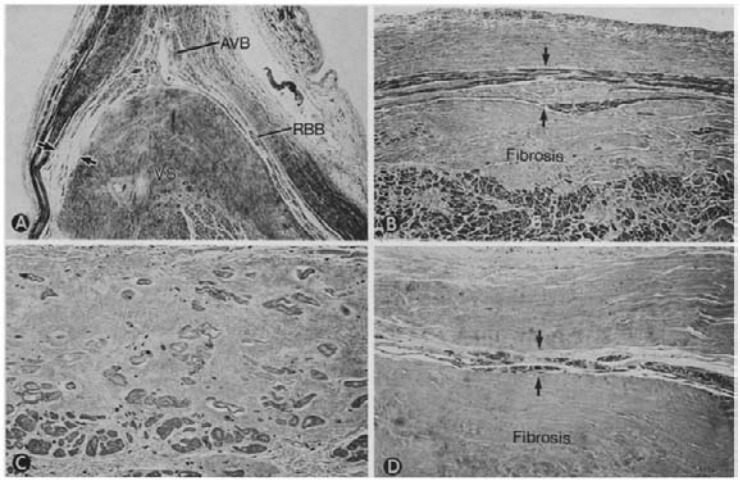

Figure 5. Case 7. Histopathology of bundle branches in myotonic dystrophy. Multiple lesions in a 48 year old woman, with focal interruption of left atrioventricular bundle (AVB) proximally (**A**, arrows), dense collagenous sheath and pronounced atrophy of left bundle (**B**, **arrows**), dense replacement fibrosis within left bundle tissue (**C**) and dense fibrosis surrounding severely atrophic right bundle (**D**, **arrows**). RBB = right bundle branch; VS = ventricular septum. (**A**, Masson trichrome stain, original magnification ×36, reduced by 32%; **B** through **D**, hematoxylin-eosin stain, original magnification (**B** and **D**) ×90, (**C**) ×180, reduced by 32%.)

electrophysiologic testing (10) have indicated that the standard 12 lead ECG may not be sensitive enough to detect early lesions of the cardiac conduction system in patients with myotonic dystrophy.

Bharati et al. (3) found mononuclear infiltrates in the sinus node and left and right bundle branches of one patient and in the approaches to the sinus node of another. In the present series of 12 cases, small clusters of lymphocytes were observed in the conduction system in three cases and involved the sinus node in two, AV node in one, AV bundle in three, left bundle branch in one and right bundle branch in two. In one of these (Case 3), inflammation of the AV node and right bundle branch was considered to be due to coexistent varicella myocarditis. In the other two cases, however, lymphocytic infiltrates were considered to represent part of the spectrum of histopathologic lesions in myotonic dystrophy. Whether the lymphocytes were causing myocyte injury or were simply responding to it is unclear.

Causes of death. Death is generally related to cardiopulmonary causes and, in the present series of 12 cases, was due to respiratory failure in 2, bronchopneumonia in 2 and pulmonary embolus in 2. In two cases, death was not directly related to myotonic dystrophy. In one, death was associated with varicella myocarditis, and in the other it was due to hemopericardium and cardiac tamponade that resulted from rupture of an acute myocardial infarction.

Sudden death occurred in 4 (33%) of the 12 cases in the present study, and in 2 of the 4, death occurred within 24 h of an operative procedure—a well recognized risk in myotonic dystrophy (45). Among 30 previously reported autopsy cases, sudden death occurred in 5 (17%) and was attributed to ventricular arrhythmias or third degree heart block (2,3,11,16,19,21,25–28,31,32,35,37–40). Thus, cardiac involvement in myotonic dystrophy occurs relatively frequently and appears to have a predilection for multifocal fibrotic and degenerative lesions of the conduction system. The resulting rhythm disturbances may be life threatening.

Table 3. Pathologic Findings of Cardiac Conduction System in Five Reported Cases of Myotonic Dystrophy

Source and Reference	Sex & Age (yr)	Sinus Node	AV Node	Penetrating AV Bundle	Branching AV Bundle	Left Bundle Branch	Right Bundle Branch
Bharati et al. (1984) (3)	F, 35	Perinodal fibrosis, mononuclear cells	Normal	Fragmentation	Fibrosis, fat, atrophy	Fibrosis, atrophy, degeneration	Fibrosis, fat, atrophy
Kennel et al. (1974) (16)	F, 55	Fibrosis, fat	Fibrosis, fat	Fibrosis, fat	Fibrosis, fat	Fibrosis, fat	Fibrosis, fat
Cannon (1962) (31)	M, 60	Not examined	Normal	Normal	Normal	Normal	Normal
Bharati et al. (1984) (3)	M, 67	Degeneration, mononuclear cells	Fibrosis	Fibrosis, atrophy	Atrophy	Fibrosis, mononuclear cells	Fibrosis, atrophy, degeneration, mononuclear cells
Thomson (1968) (21)	F, 69	Fibrosis, degeneration	Fibrosis, degeneration	Fibrosis	Fibrosis	Degeneration	Fibrosis, atrophy, degeneration

Abbreviations as in Table 1.

References

1. Hiromasa S, Ikeda T, Kubota K, et al. A family with myotonic dystrophy associated with diffuse cardiac conduction disturbances as demonstrated by His bundle electrocardiography. Am Heart J 1986;111:85–91.
2. Grigg LE, Chan W, Mond HG, Vohra JK, Downey WF. Ventricular tachycardia and sudden death in myotonic dystrophy: clinical, electrophysiologic and pathologic features. J Am Coll Cardiol 1985;6:254–6.
3. Bharati S, Bump FT, Bauernfeind R, Lev M. Dystrophica myotonia: correlative electrocardiographic, electrophysiologic, and conduction system study. Chest 1984;86:444–50.
4. Perloff JK, Stevenson WG, Roberts NK, Cabeen W, Weiss J. Cardiac involvement in myotonic muscular dystrophy (Steinert's disease): a prospective study of 25 patients. Am J Cardiol 1984;54:1074–81.
5. Hawley RJ, Gottdiener JS, Gay JA, Engel WK. Families with myotonic dystrophy with and without cardiac involvement. Arch Intern Med 1983;143:2134–6.
6. Gottdiener JS, Hawley RJ, Gay JA, DiBianco R, Fletcher RD, Engel WK. Left ventricular relaxation, mitral valve prolapse, and intracardiac conduction in myotonia atrophica: assessment by digitized echocardiography and noninvasive His bundle recording. Am Heart J 1982;104:77–85.
7. Atarashi H, Saito H, Aoki H, Hayakawa H. A case of myotonic dystrophy associated with sick sinus syndrome. Jpn Circ J 1981;45:763–8.
8. Komajda M, Frank R, Vedel J, Fontaine G, Petitot JC, Grosgogeat Y. Intracardiac conduction defects in dystrophia myotonica: electrophysiological study of 12 cases. Br Heart J 1980;43:315–20.
9. Motta J, Guilleminault C, Billingham M, Barry W, Mason J. Cardiac abnormalities in myotonic dystrophy: electrophysiologic and histopathologic studies. Am J Med 1979;67:467–73.
10. Prystowsky EN, Pritchett EL, Roses AD, Gallagher J. The natural history of conduction system disease in myotonic muscular dystrophy as determined by serial electrophysiologic studies. Circulation 1979;60:1360–4.
11. Franks AJ. Cardiac pathology in chronic myopathy, with particular reference to dystrophia myotonica. J Pathol 1978;125:213–7.
12. Ludatscher RM, Kerner H, Amikam S, Gellei B. Myotonia dystrophica with heart involvement: an electron microscopic study of skeletal, cardiac, and smooth muscle. J Clin Pathol 1978;31:1057–64.
13. Venco A, Saviotti M, Besana D, Finardi G, Lanzi G. Noninvasive assessment of left ventricular function in myotonic muscular dystrophy. Br Heart J 1978;40:1262–6.
14. Clements SD, Jr., Colmers RA, Hurst JW. Myotonia dystrophica: ventricular arrhythmias, intraventricular conduction abnormalities, atrioventricular block and Stokes-Adams attacks successfully treated with permanent transvenous pacemaker. Am J Cardiol 1976;37:933–5.
15. Griggs RC, Davis RJ, Anderson DC, Dove JT. Cardiac conduction in myotonic dystrophy. Am J Med 1975;59:37–42.
16. Kennel AJ, Titus JL, Merideth J. Pathologic findings in the atrioventricular conduction system in myotonic dystrophy. Mayo Clin Proc 1974;49:838–42.
17. Uemura N, Tanaka H, Niimura T, et al. Electrophysiological and histological abnormalities of the heart in myotonic dystrophy. Am Heart J 1973;86:616–74.
18. Tanaka N, Tanaka H, Takeda M, Nimura T, Kanehisa T, Terashi S. Cardiomyopathy in myotonic dystrophy: a light and electron microscopic study of the myocardium. Jpn Heart J 1973;14:202–12.
19. Rausing A. Focal myocarditis in familial dystrophia myotonica. Br Heart J 1972;34:1292–4.
20. Bache RJ, Sarosi GA. Myotonia atrophica: diagnosis in patient with complete heart block and Stokes-Adams syncope. Arch Intern Med 1968;121:369–72.
21. Thomson AM. Dystrophia cordis myotonica studied by serial histology of the pacemaker and conducting system. J Pathol Bacteriol 1968;96:285–95.
22. Church SC. The heart in myotonia atrophica. Arch Intern Med 1967;119:176–81.
23. Bulloch RT, Davis JL, Hara M. Dystrophia myotonica with heart block: a light and electron microscopic study. Arch Pathol 1967;84:130–40.
24. Wolintz AH, Sonnenblick EH, Engel WK. Stokes-Adams syndrome and atrial arrhythmias as the presenting symptoms of myotonic dystrophy, with response to electrocardioversion. Ann Intern Med 1966;65:1260–6.
25. Árnason G, Berge T, Dahlberg L. Myocardial changes in dystrophia myotonica. Acta Med Scand 1964;176:535–8.
26. Holt JM, Lambert EHN. Heart disease as the presenting feature in myotonia atrophica. Br Heart J 1964;26:433–6.
27. Biörck G, Stigell P. Dystrophia myotonica: a follow-up study of a family with associated heart disease. Acta Med Scand 1964;175:395–9.
28. Örndahl G, Thulesius O, Enestrom S, Dehlin O. The heart in myotonic disease. Acta Med Scand 1964;176:479–91.
29. Petkovich NJ, Dunn M, Reed W. Myotonia dystrophica with A-V dissociation and Stokes-Adams attacks: a case report and review of the literature. Am Heart J 1964;68:391–6.
30. Payne CA, Greenfield JC Jr. Electrocardiographic abnormalities associated with myotonic dystrophy. Am Heart J 1963;65:436–40.

31. Cannon PJ. The heart and lungs in myotonic muscular dystrophy. Am J Med 1962;32:765–75.

32. Fisch C, Evans PV. The heart in dystrophia myotonica: report of an autopsied case. N Engl J Med 1954;251:527–9.

33. Litchfield JA. A-V dissociation in dystrophia myotonica. Br Heart J 1953;15:357–9.

34. Fisch C. The heart in dystrophia myotonica. Am Heart J 1951;41:525–38.

35. Wohlfart G. Dystrophia myotonica and myotonia congenita: histopathologic studies with special reference to changes in the muscles. J Neuropathol Exp Neurol 1951;10:109–24.

36. DeWind LT, Jones RJ. Cardiovascular observations in dystrophia myotonica. JAMA 1950;144:299–303.

37. Black WC, Ravin A. Studies in dystrophia myotonica. VII. Autopsy observations in five cases. Arch Pathol 1947;44:176–91.

38. Fogin ID. Dystrophia myotonica: report of two cases, with associated hyperostosis frontalis interna in one. J Mich Med Soc 1946;45:500–3.

39. Keschner M, Davison C. Dystrophia myotonica: a clinicopathologic study. Arch Neurol Psychiat 1933;30:1259–75.

40. Adie WJ, Greenfield JG. Dystrophia myotonica (myotonia atrophica). Brain 1923;46:73–127.

41. Davies MJ, Anderson RH, Becker AE. The Conduction System of the Heart. London: Butterworths, 1983:9–56.

42. James TN, Sherf L, Schlant RC, Silverman ME. Anatomy of the heart. In: Hurst JW, Logue RB, Rackley CE, et al., eds. The Heart: Arteries and Veins. 5th ed. New York: McGraw-Hill, 1982:22–74.

43. Hudson REB. The conducting system: anatomy, histology, pathology in acquired heart disease. In: Silver MD, ed. Cardiovascular Pathology. Vol. 1. New York: Churchill Livingstone, 1983:633–82.

44. Lev M. The conduction system. In: Gould SE, ed. Pathology of the Heart and Blood Vessels. 3rd ed. Springfield, Il: Charles C Thomas, 1968:180–220.

45. Mudge BJ, Taylor PB, Vanderspek AF. Perioperative hazards in myotonic dystrophy. Anaesthesia 1980;35:492–5.