The Heart in Progressive Muscular Dystrophy

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A case of progressive muscular dystrophy with cardiac involvement in a young Negro man is reported. The presenting problem was cardiomegaly and congestive heart failure. It was not until compensation was achieved that the underlying myopathy became apparent. Death was unexpected and presumably sudden. An unusual finding at the postmortem examination was the marked thickening of the endocardium. The literature in regard to the clinical and pathologic manifestations of cardiac involvement in this myopathy is reviewed.

Ordinarily, the presence of heart failure is readily recognized. However, the nature of the underlying disease affecting the heart is often not discernible. Recently, we were confronted with the problem of heart failure in a patient who was presumed to have “idiopathic cardiomegaly.” It was not until cardiac compensation was achieved that the nature of the underlying disease, namely, progressive muscular dystrophy, became apparent.

This paper emphasizes the occurrence of cardiac involvement in progressive muscular dystrophy by (1) reporting case and (2) reviewing the literature in regard to the cardiac manifestations in this myopathy.

Case Report

L. L., a 30 year old Negro man, was referred to the Temple University Hospital because of increasing shortness of breath and swelling of the ankles. About one and one-half years ago, he began to experience easy fatigability and nocturnal attacks of shortness of breath. Occasionally, he complained of palpitation and painful sensations around the heart. Digitalis was prescribed by his physician one year ago. He took the drug at irregular intervals thereafter. During the past month, he noticed swelling of his ankles and increasing shortness of breath.

Systematic inquiry revealed that at the age of 13, he was seen in the Temple University Outpatient Cardiac Clinic because of pain in the ankle joints. Unfortunately, his record contained only an electrocardiogram which presented no abnormality. At the age of 21, during a routine pre-enlistment Army examination, he was told that he had a “leaky” heart and was advised to limit his activities. Since then, he had worked part-time as an attendant at a baseball park. Several years ago, he was told that he had high blood pressure.

Physical examination revealed a well developed Negro man appearing younger than his stated age. He was exceedingly apprehensive, manifesting outspoken fright. Dyspnea, orthopnea, and cervical venous distention were present. Repeated determinations of the blood pressure varied from 100-150/70-112. The ocular fundi were normal. The point of maximal impulse was in the sixth intercostal space at the left midaxillary line. Cardiac dullness extended 7 cm. to the right of the midsternal line in the fourth intercostal space and 9 cm. to the left of the midsternal line in the third intercostal space. The ventricular rate was 120 per minute with a pulse defect of 20 per minute. There was usually an irregular rhythm. Occasionally, a rapid regular rhythm with frequent extrasystoles occurred. The mitral first sound was decreased in intensity and the pulmonary second sound was accentuated. In the left lateral recumbent position, a soft low-pitched systolic murmur replacing the mitral first sound was audible. Examination of the lungs revealed dullness over the right lower lobe with decreased breath and voice sounds and bilateral basilar subcrepitant rales. The liver was palpated 4 cm. below the right costal cage and was not tender. Pitting edema of the legs was present. The usual therapeutic regimen employed in the management of congestive heart failure was instituted.

Following subsidence of the edema, it was noticed that his calf and arm muscles were unusually prominent. When allowed to ambulate, his gait was observed to be awkward, hesitant, and jerky. Upon arising from a sitting position on the floor, he would climb up his legs. There was weakness of the muscles in spite of their prominence. Neurologic consultation (Dr. S. F. Gilpin, Jr.) supported the diagnosis of progressive muscular dystrophy. This was confirmed by a right gastrocnemius muscle biopsy (fig. 1).

Examination of a 24 hour urine specimen revealed 774 mg. creatinine and 367 mg. creatine. Other laboratory studies disclosed a normal complete blood count and blood urea nitrogen and a negative serology. The sedimentation rate was 13 mm. in one hour. Repeated urinalyses disclosed the presence of proteinuria with hyaline and granular casts. The specific gravity of the urine varied from 1.010 to 1.025.

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An electrocardiogram was taken on two occasions, one a day after admission, the other nine days later. Both were essentially similar. The later tracing is shown in figure 2. There is a sinus tachycardia at a rate of 116 per minute with occasional premature ventricular contractions. There is evidence of auricular disease and clockwise rotation of the heart around its long axis with left ventricular hypertrophy.

Roentgenographic examination of the chest (figure 3) revealed increased bronchovascular markings of central distribution indicating pulmonary congestion. There was marked enlargement of the heart, predominantly of the left ventricle. Left auricular enlargement was demonstrated by the double shadow within the right heart border and by displacement of the barium-filled esophagus.

Clinically, the patient was responding satisfactorily to treatment. Arrangements were being made for his discharge. Early one morning, 19 days after admission, the patient was found dead by a nurse on her routine ward rounds.

**Autopsy Findings**

Gross examination of the gastrocnemius and related calf muscles showed them to be flabby, yellow and greasy. Compared with these muscles, those of the thigh, trunk and arm appeared normally red and of decidedly better tone. It is of interest that the stomach contained approximately 200 cc. of fresh blood. Three of the 4 cases reported by Bevan also had gastric bleeding. Our case had neither frank ulcers nor perforations.

From a survey, both gross and microscopic, of the tissues after death, it seems probable that the patient died of sudden cardiac arrest. All sections showed the effect of longstanding congestion with a terminal acute exacerbation. In addition there were antemortem thrombi in both auricles and old and recent infarcts in the spleen and in both kidneys, dramatic proof that the cardiac injury was old.

The appearance of the heart itself was of greatest interest. It was enlarged by both dilatation and hypertrophy and both sides were about equally

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**Fig. 1.** Photomicrograph of skeletal muscle in cross section (220 x). Most of the fibers reveal extreme hypertrophy. Interspersed are the very small, atrophic or hypogenetic fibers.

**Fig. 2.** Electrocardiogram (1/21/50) revealing auricular disease and clockwise rotation of the heart around its long axis with left ventricular hypertrophy.
involved. The heart weighed 650 Gm. The wall of the left ventricle measured 2 cm. in its thickest area. The linings of the pericardial cavity were normal in appearance. The coronary vessels were without evidence of atherosclerosis and they were of normal size and pattern. There was no evidence that the changes found in the myocardium were due to a deficient blood supply. The myocardium of both ventricles was firm and tough. When sectioned tangentially it was found to be laced and mottled with fine, gray striae and patches which resembled fibrous tissue. There were no delineated areas suggesting infarction. The left ventricular cavity was lined by a layer of smooth, yellowish-gray tissue measuring up to 1 mm. in thickness. The appearance was somewhat similar to that of fetal endocarditis. Three of Bevan’s cases showed this same alteration. There was a smooth thickening of the distal edges of the leaflets of both mitral and tricuspid valves, but the appearance was not characteristic of that of
healed rheumatic valvulitis nor was the process extensive enough to cause a major disturbance in valve efficiency. The tricuspid valve ring was relaxed, measuring 14 cm. in circumference. The aortic valve ring circumference was less than normal, measuring 5 cm. This, coupled with the thickened endocardium, made one think of the possible relationship of this condition to fetal endocarditis in which the same cardiac lesions are sometimes found.

On microscopic examination the changes in the skeletal muscles were definite but not so severe nor so extensive as those of most cases of pseudohypertrophic muscular dystrophy. Giant hypertrophied fibers were occasionally found and there were scattered small areas in which the fibers had atrophied to approximately one fourth their normal size. Striations were quite sharply and clearly delineated as one expects them to be in this condition but there were focal condensations of sarcoplasm. Sarcolemmal nuclear proliferation was striking in some areas. The sections contained an abnormal amount of adult fat.

The changes in the myocardium were much more striking than those in the skeletal muscle. Here there were areas of recent degenerative change with accompanying exudative inflammatory reaction (fig. 4). There were irregular lines and patches of fibrous tissue through every section and almost every field. There was little, if any, excess fat in the myocardium. The striations were blurred and fuzzy. The endocardium and valve leaflets were considerably thickened by masses of collagenous tissues which were relatively acellular (fig. 5). Stains for elasticum showed little change in amount or distribution of that substance.

**Discussion**

When confronted with cardiomegaly, one ordinarily thinks of hypertensive, valvular, or congenital heart disease. Rarer causes include primary amyloidosis, glycogenosis, and beriberi. However, there are many of these cases for which no etiologic factor is, at present, apparent. These constitute the group known as "idiopathic cardiomegaly." The recent literature attests to the frequency with which this diagnosis is being made.1,2 With increasing knowledge, many cases will be separated from this group, as has recently been done by Evans.3 Our patient had cardiomegaly and congestive heart failure. It was not until he was compensated and allowed to ambulate that the nature of the underlying disease became apparent.

Progressive muscular dystrophy usually develops in infancy or early childhood but may arise at any time from birth to adult life.3-7 The earlier the onset, the more rapid the clinical course.8 Males are more frequently affected than females.9 Cases in Negroes have been described.9-11 It is a disease affecting all types of muscle tissue.12 In addition, there may be changes in the skin, bone, and endocrine glands.12-14 Involvement of the skeletal muscle, however, results in the prominent and well known manifestations of this disease.12,14,16

The incidence of cardiac involvement in progressive muscular dystrophy is not known. In fact, in none of the modern texts nor in the recent literature has there been an attempt to estimate the incidence of the disease per se. In 1931, Hough17 roughly estimated the incidence of this myopathy as being approximately 6 per 100,000 population. Meerwein18 collected 480 cases of progressive muscular dystrophy published before 1904. In 89 of these, there was noted some abnormality of the heart or pulse. In our review, with particular emphasis on the literature since Globus’ report in 1922,19 we have encountered a total of 292 cases. In 156 of these, nothing was stated in regard to the cardiovascular system. In 42 cases, whatever cardiovascular data were presented (usually meager) were normal. In 94 cases, whatever cardiovascular data were presented, whether clinical, radiologic, electrocardiographic, or postmortem, were abnormal. These figures are cited only to indicate the fact that the cardiovascular system is involved in progressive muscular dystrophy in a considerable percentage of cases. A more specific conclusion cannot be made from these data because, first, our interest was directed particularly to cardiovascular abnormalities, and second, cases are usually reported in a manner dependent upon the interest of the observer. It should be noted that in cursory observations by previous workers, opinions as to the incidence of cardiac involvement in this myopathy have varied from one of doubt as to its very occurrence to one in which it was thought to be present sooner or later in every case.20,21

The most prominent symptoms of cardiac involvement in progressive muscular dystrophy...
appear to be related to the arrhythmias which frequently occur in these patients. They may be perfectly well and then suddenly feel sick, experience palpitation, and then break out in a cold sweat, accompanied at times by vomiting and abdominal pain. Not infrequently, there may be a sudden shock-like state, either without apparent cause or following minor stimuli, terminating equally abruptly either in recovery or death. Gastrointestinal complaints may occasionally predominate to a degree warranting an exploratory laparotomy. In one such instance, death occurred postoperatively, presumably as a result of a cardiac arrhythmia. There may be recurrent bouts of fever and tachycardia, with or without gastrointestinal symptoms. The daily variations in the temperature curve may be exaggerated. A few may be dyspneic. Swelling of the legs was rarely noted. Two patients had precordial pain. It is to be emphasized that some of these patients offer no complaints until the attending physician, faced with electrocardiographic evidence of an arrhythmia as the sole evidence of heart disease, inquires and discovers that periodic palpitations have been frequently experienced.

A statement in regard to the clinical evaluation of heart size was noted in 38 instances. In 6 of these the heart was found to be enlarged. The sounds were usually of good quality. Hurwitz observed a slurred first heart sound and Boas and Lowenburg emphasized the presence of a feeble first heart sound at the apex and an accentuated second sound at the base. Bert and Barat heard an opening snap with duplication of the first heart sound, confirmed by phonocardiography. Murmurs were present in a few instances. These were usually systolic in time and soft in character, located at the apex or base of the heart. In a case of Bevan's, the murmur was harsh. Two patients had rheumatic heart disease and mitral stenosis. In one instance, a gallop rhythm was intermittently present. In 2 patients with precordial pain, auscultation revealed a pericardial friction rub in one, and mitral stenosis in the other.

The blood pressure was recorded in only 24 instances. In 10 patients either the systolic or diastolic or both were elevated. Another patient, a 24 year old male, had a past history of hypertension. Of these 11 patients, 7 were below the age of 40 years. In 5 patients, 10 years of age or less, the blood pressure was within normal limits. In the remaining patients, the blood pressure ranged from 100-130/50-84. Funduscopic examination was done in 7 cases, being normal in 6 of these. In the patient who had a history of hypertension, the retinal arterioles were narrowed. In view of these data, it is remarkable that some have regarded a hypotensive state as an almost constant finding.

Boas and Lowenburg studied the heart rate of 7 patients with progressive muscular dystrophy by means of a cardiotachometer. The striking feature noted was the tachycardia evident in each of these patients both waking and sleeping. The absence of the normal drop in pulse rate during sleep was confirmed by Kraus. Another characteristic finding was the lability of the heart rate, accelerating excessively in response to minimal stimuli.

In our review, a notation regarding the clinical rate or rhythm was found in 27 instances. The rate was recorded in 12 and varied from 80 to 180 per minute. A few of those with the slower rates had periods during which the pulse rate was increased. In 8 patients there was observed either an irregular pulse or periods of rapid heart action. In one of the patients, the pulse suddenly became irregular at a rate of 160 per minute. Pressure on the "right vagus" resulted in a temporary cessation of this arrhythmia. Interestingly, the sudden onset of these rapid arrhythmias was often related to minor stimuli, such as a scolding or a tooth extraction.

The results of x-ray examination of the heart were noted in 25 instances. In one, the size of the heart was indeterminate; in another, the cardiac silhouette was "ball-shaped." In the others, the heart was found to be enlarged, either slightly or in all diameters. In one patient, the esophagea-
gus was slightly displaced by an enlarged right auricle.\textsuperscript{9} A kymographic study was done in this patient and small excursions were observed.

Electrocardiographic observations were recorded in 105 instances. The rate was usually rapid with normal or irregular sinus rhythm (sinus arrhythmia). Extrasystoles, either auricular or ventricular in origin, were not infrequent. In one patient, ventricular extrasystoles occurred in bigeminy.\textsuperscript{22} Two had paroxysmal ventricular tachycardia.\textsuperscript{21, 22} The P wave was of increased amplitude in leads II and III in a patient with progressive muscular dystrophy who also had rheumatic heart disease and mitral stenosis.\textsuperscript{25} In another, the P wave was 4 mm. in amplitude in lead II.\textsuperscript{38} The P-R interval was normal in all but 3 cases.\textsuperscript{21, 22, 28} In 2, the P-R interval was longer than 0.20 second \textsuperscript{21, 22}; in another, a Wolff-Parkinson-White syndrome was present.\textsuperscript{26} The duration of the QRS complex was prolonged in 3.\textsuperscript{22, 27, 28} Lengthening of the Q-T interval was observed once.\textsuperscript{39}

As is true of the early electrocardiographic literature, much emphasis was placed on the configuration of the QRS complex in the limb leads. The mean electrical axis of the QRS complex was usually normal, occasionally deviated either to the right or to the left.\textsuperscript{41} A Q wave was frequently found, particularly in leads II and III.\textsuperscript{38} These were carefully compared with the Q wave of Pardee, the author concluding that they probably denoted myocardial involvement not otherwise apparent.\textsuperscript{28} There was not one instance of an abnormally wide Q wave. In one patient, after the development of precordial pain accompanied by a friction rub, the Q wave in lead I increased.\textsuperscript{24} The R wave was frequently of increased voltage in leads I and II, and low or absent in lead III.\textsuperscript{24, 38} Occasionally, it was notched, slurred, or thickened.\textsuperscript{24} The S-T interval was often abbreviated, there being an early takeoff of T.\textsuperscript{38} Occasionally, the S-T segment was slightly elevated in the limb leads, particularly in leads I and II; infrequently, it was slightly depressed in lead III.\textsuperscript{24, 38}

In leads I and II, the T wave was usually upright, occasionally quite tall and peaked, rarely low positive. The T wave in lead III was frequently flattened or inverted.\textsuperscript{38} In the one study in which it was stated that precordial leads were employed, CF\textsubscript{2} and IV\textsubscript{F} were chosen.\textsuperscript{25} These revealed nothing of note.

Globus,\textsuperscript{19} in a review of the literature to 1922, summarized the postmortem findings of the heart in 10 cases of progressive muscular dystrophy and reported an additional case. He was particularly interested in determining the relationship of the heart changes in this myopathy to a possible acute intercurrent disease or to some past illness. All showed fairly definite myocardial disease of varying degree. He concluded that infection was insufficient to explain the diffuse nature and the morphologic character of the myocardial involvement.

In a review of the literature since 1922, we were able to find 19 additional cases in which necropsies were done and reported in whole or in part. The ages at death varied from 10 years to 67 years, the average being 25.4 years. All but one were males.

Death occurred suddenly in 2 cases,\textsuperscript{49} within 35 minutes in another,\textsuperscript{22} within three hours in 1,\textsuperscript{29} within 48 hours in 2,\textsuperscript{27, 32} and on the second to fourth postoperative day in 3.\textsuperscript{9, 22, 23} The two deaths which occurred suddenly were attributed to "edema of the larynx-status lymphatics."\textsuperscript{79} Twelve patients died shortly after development of a respiratory infection. In one, death followed respiratory paralysis.\textsuperscript{32} One died of acute left ventricular failure.\textsuperscript{32} In one, "disturbances of the heart" developed, resulting in the patient's death.\textsuperscript{31} Another died during a bout of diarrhea, fever, and tachycardia of 180 beats per minute.\textsuperscript{9}

The weight of the heart was recorded in 7 instances and varied from 140 Gm. to 600 Gm., four hearts weighing 190 Gm. or less,\textsuperscript{9, 41} and three weighing 285 Gm. or more,\textsuperscript{9, 25, 27} In an additional case, it is stated that the heart was hypertrophied.\textsuperscript{32} In 4, there was dilatation.\textsuperscript{21, 40, 41} and, in one, a striking bulge of the left ventricle was observed.\textsuperscript{42}

The epicardial fat was increased in some and, at times, found to "invade" the myocardium. Occasionally, areas of heart muscle were replaced by connective tissue. The ventricular
wall was usually streaked with greyish flecks and small fibrotic areas were frequently recognized. The muscle tone was usually increased; occasionally, the wall was flabby. The endocardium grossly was normal or slightly thickened. Mural thrombi were observed in only one case. The valves were not involved. The coronary blood vessels were patent in all but one. The latter, a 61 year old male, had extensive arteriosclerosis with old occlusions of both branches of the left coronary artery.

Microscopically, fibrosis of the myocardium was observed, varying from a finely diffuse sclerosis to large areas of scarring. There was usually fatty infiltration and edema not only of the interstitial tissue but also of the muscle. The muscle fibers varied in size. In some instances they had undergone degeneration and were replaced by connective tissue. There was fragmentation, loss of striation, and condensation of cytoplasm. The nuclei showed degenerative changes. In some cases there was a diffuse but sparse infiltration of the myocardium with wandering cells and histiocytes. No evidence of a specific inflammatory reaction was present. The endocardium, microscopically, was usually normal; occasionally, it was found to be slightly thickened in a few small areas.

An unusual feature in our case was the thickening of the endocardium. Idiopathic hypertrophy of the heart with endocardial fibrosis has been reported in infants.46 According to Kugel and Stoloff,47 the true form of idiopathic congenital cardiac hypertrophy reveals no myocardial fibrosis. Weisman48 has reported 2 such cases. In Mahon’s case,49 there were fibrotic and degenerative myocardial changes, but associated lesions were present to suggest an inflammatory origin.

The various changes in the reported cases were more extensive in the left ventricle than in the right. Although the coronary vessels were usually free of disease, a few observers noted small intimal atheromas.9, 20 These were sometimes found in the aorta also.9 The aorta was occasionally found to be smaller than normal.27 Thromboembolic disease was observed in 3 instances.7, 27, 28 Chronic passive congestion was infrequently noted, owing probably to the early demise of these patients.

As has been emphasized by others, more of these cases will be recognized if a sense of awareness is maintained. The peculiar gait, large calves, and “climbing up the legs” (Gower’s sign) constitute an important triad in the diagnosis of progressive muscular dystrophy. A labile and rapid pulse rate, an arrhythmia, or an abnormal character of the heart sounds suggest cardiac involvement, which may be confirmed by electrocardiographic study.

SUMMARY

The occurrence of cardiac involvement in progressive muscular dystrophy is emphasized by (1) reporting a case of a young Negro man with cardiomegaly in whom the underlying myopathy was masked by heart failure and (2) summarizing the literature in regard to the clinical, electrocardiographic, radiographic, and pathologic manifestations.

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