Progressive Muscular Dystrophy

Hemodynamic, Angiographic, and Pathologic Study of a Patient with Myocardial Involvement

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SUMMARY
This paper describes the case of a young man with progressive muscular dystrophy who had supraventricular arrhythmias and intractable congestive failure. Hemodynamic studies and left cineventriculographic findings were compatible with a diagnosis of severe left ventricular failure.

Coronary cinearteriography showed an abrupt ending of the artery to the sino-atrial node. At necropsy, a noninflammatory degeneration was found in this particular vessel. The pathogenesis of the cardiac arrhythmias seen in this condition is discussed in the light of these cineangiographic and histopathologic observations.

Additional Indexing Words:
Supraventricular arrhythmia
Cinecoronary arteriograms

Cardiac involvement is a common complication of progressive muscular dystrophy of the Duchenne type. Several reports have emphasized the frequent appearance of tachycardia,1-3 arrhythmias,2 4 and congestive cardiac failure.5 7 Others have described the multiple electrocardiographic abnormalities often seen among these patients.3 5 6 8 9 Latent congestive failure may be present in some cases without overt signs of cardiac decompensation. It can be unmasked and substantiated by hemodynamic studies before and during exercise.10

Despite the frequency of myocardial involvement, review of the literature yields only a small number of hemodynamic studies limited to the right cardiac chambers and the pulmonary circuit.3 10 11-14 The purpose of this case report is to present the hemodynamic disturbances observed at right and left heart catheterization. Coronary cinearteriograms were done to correlate the angiographic findings with those of the postmortem examination.

Report of Case
An 18-year-old white male was referred for cardiac evaluation because of severe congestive failure. Progressive muscular dystrophy of the Duchenne type had been diagnosed at the age of 10 years. The patient had remained ambulatory and fairly active until 5 months prior to the present study. At that time, his sleep was frequently disturbed by a persistent dry cough. During the following 2 or 3 weeks, he became progressively short of breath with smaller amounts of exertion. He also complained of retrosternal pain which he described as a sensation of pressure. This pain was induced by exertion and relieved by rest. These symptoms became steadily worse until finally the patient could sleep only in a sitting position.

On April 22, 1967, 2 months after the onset of these symptoms, he was admitted to another hospital. Physical examination revealed signs of left and right congestive failure. During the following 3 weeks, the patient’s condition improved steadily with rest in bed, digitalis, and diuretics. He was discharged on May 14, 1967.

This improvement, however, was short-lived, and the recurring manifestations of congestive failure necessitated his admission again to the same hospital during the first week in July. He
responded poorly to the usual therapeutic measures. He was then transferred for further cardiac evaluation.

Physical examination revealed marked and symmetrical atrophy of the following muscles: deltoid (upper portion), triceps, biceps radii, quadriceps femori, tibial, and peroneal groups. The gastrocnemius and soleus muscles were enlarged. Contractures of the elbows and ankles were present.

The cardiac apical impulse was diffuse and felt at the anterior left axillary line in the sixth intercostal space. The cardiac sounds were of poor quality; a diastolic gallop and a holosystolic murmur, grade II/VI, were best heard at the apex. A few inspiratory rales were disseminated over both lung bases. The liver edge was felt 3 fingerbreadths below the right costal margin. The neck veins were engorged and pulsating at 30° of angulation.

The chest x-rays and barium swallow (fig. 1) showed generalized cardiac enlargement with indentation of the esophagus by the dilated left atrium. The transverse cardiac diameter was 18 cm or 50% above the expected value for a patient of this height and weight. The electrocardiogram (fig. 2) showed atrial fibrillation with a ventricular rate of approximately 80 beats/min, left axis deviation, and intraventricular conduction defect. R waves were absent in leads III, aVF, and V2 to V5. The phonocardiogram confirmed the presence of a holosystolic murmur of moderate intensity, best recorded at the apex. The intensity of the first mitral sound was decreased. The vectorcardiogram (cube system, fig. 3) showed the abnormal inscription and rotation of the QRS se loop in the three planes. The S-T segment was directed to the right anteriorly and inferiorly, and the QRS-T angle was very wide.

The hemodynamic data obtained at right and left cardiac catheterization are presented in table 1. The mean right atrial and pulmonary wedge pressures and the end-diastolic ventricular pressures were markedly elevated. The rise in pulmonary and right ventricular systolic pressures were moderate. The arterial O2 saturation was decreased to 89%. The cardiac output and index were definitely below the normal range, but the pulmonary arteriolar resistance was not elevated. No shunt was detected by indicator-dilution curve.

The left ventriculogram revealed a severely dilated chamber which contracted poorly and emptied slowly. There was mild mitral regurgitation. Both coronary arteries were opacified by the selective technic.15 The lumina of the main trunk and the visualized branches were very smooth (fig. 4A and B). No obstruction or narrowing could be demonstrated. The number of branches

![Figure 1](http://circ.ahajournals.org/)

Chest x-rays. There is marked generalized cardiac enlargement. The transverse cardiac diameter is 18 cm or 50% above the predicted average for this patient.

* Simultaneous recordings.

### Table 1

<table>
<thead>
<tr>
<th>Hemodynamic Data</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressures (mm Hg)</td>
<td></td>
</tr>
<tr>
<td>Right atrium, mean</td>
<td>32</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>62/15</td>
</tr>
<tr>
<td>End diastolic</td>
<td>32</td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>60/35</td>
</tr>
<tr>
<td>Mean</td>
<td>40</td>
</tr>
<tr>
<td>Pulmonary wedge, mean</td>
<td>43*</td>
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<tr>
<td>Left ventricle</td>
<td>120/12</td>
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<tr>
<td>End diastolic</td>
<td>42*</td>
</tr>
<tr>
<td>Ascending aorta</td>
<td>115/80</td>
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<tr>
<td>Mean</td>
<td>95</td>
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<tr>
<td>Heart rate (/min)</td>
<td>100</td>
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<tr>
<td>O2 content (vol %)</td>
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<tr>
<td>Arterial</td>
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<tr>
<td>Pulmonary artery</td>
<td>10.0</td>
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<tr>
<td>Oxygen consumption (cc/min)</td>
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<tr>
<td>Cardiac output (L/min)</td>
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</tr>
<tr>
<td>Cardiac index</td>
<td>2.3</td>
</tr>
<tr>
<td>Stroke volume (cc/beat)</td>
<td>35</td>
</tr>
<tr>
<td>Stroke index</td>
<td>23</td>
</tr>
<tr>
<td>Pulmonary arteriolar resistance (dynes sec cm⁻⁵)</td>
<td>138</td>
</tr>
</tbody>
</table>
Electrocardiogram. The QRS axis is markedly deviated to the left. P waves are absent (atrial fibrillation). Slurring in the inscription of the QRS complex and slight prolongation of its duration (0.11 sec) are compatible with an intraventricular conduction defect. The R wave is embryonic in leads II and V₁ and missing in leads III, aVF, and V₂ to V₅. This could be interpreted as the result of a remote anteroseptal and posteroinferior myocardial infarction.

Two months later, the patient was readmitted, because of severe, constant pain over the right side of the abdomen. The liver edge was pulsating and was felt at the right iliac crest. He failed to respond to treatment and expired 2 weeks later, approximately 6 months after the onset of overt congestive failure.

At autopsy, the heart appeared markedly dilated and weighed 400 g. The left ventricular wall was 1.1 cm thick and the right ventricular wall was 0.3 cm thick. The mitral valve was free of rheumatic involvement. Gross examination of the coronary arterial trunks and of their main branches failed to reveal any significant atherosclerotic changes. There were no intimal plaques. Evidence for recent or remote thrombosis was lacking. Multiple sections throughout the myocardium showed numerous foci of whitish-gray fibrous tissue distributed throughout the whole organ as well as through several areas of marked...
Figure 3
Vectorcardiogram. The QRS sE loop is deviated superiorly, to the left, and posteriorly. The initial and terminal portions show delayed conduction. The S-T segment is directed to the right anteriorly and the T loop is discordant. The P sE loop is absent. F = frontal plane; H = horizontal plane; S = sagittal plane.

Figure 4
(A and B) Coronary cinearteriograms (35-mm film; 6-inch intensifier). (A) Right coronary artery opacified in a slight left anterior oblique projection, early frame. (B) Left coronary artery opacified in the right anterior oblique projection, early frame. In both arteries, the main trunk and the visualized branches appear very smooth. The first branch of the right coronary artery ends abruptly. (C) Right cinecoronary arteriogram recorded in the right oblique projection with interposition of a "zoom lens" in front of the camera. The branch to the sinoatrial node is interpreted as ending very abruptly without previous tapering down of its lumen (arrow).

endocardial thickening involving the intraventricular septum. These were particularly abundant around the bundle of His.

Serial sections were made of the sinoatrial and the atrioventricular nodes (fig. 5A and B). The lumen of the artery coursing through the sinoatrial node was markedly narrowed. The walls of this vessel displayed abundant endothelial proliferation and widespread cystic degeneration. An elastic tissue stain showed this to be located between the internal and the external elastic laminae. Evidence of an inflammatory reaction was conspicuously absent.

Discussion
Cardiac involvement in progressive muscular dystrophy of the Duchenne variety is considered to be a common occurrence. Prevalence figures differ widely, however, ranging from 25 to 85%.5, 6, 16 Clinical manifestations include tachycardia,1-8, 10 arrhythmias2, 5, 6 murmurs,3 congestive failure,5-7 gallop rhythm,17 poor heart sounds,18 cardiomegaly,19 chest pain,20 and sudden death.7, 14, 21, 22

Perloff and associates6 called attention to
the difficulty of an accurate radiologic interpretation of the cardiac size and configuration in patients with progressive muscular dystrophy complicated by thoracic deformities and elevated diaphragms. Individuals with pectus excavatum or with loss of normal thoracic kyphosis may have a leftward shift of the cardiac silhouette and prominent pulmonary artery. The patient under discussion presented with generalized cardiac enlargement of a huge degree for which no thoracic deformities could account. Furthermore, bilateral pulmonary congestion was also in keeping with the presence of advanced cardiac failure.

An abnormal electrocardiogram, often the earliest evidence of myocardial involvement, is found in a large majority of patients with pseudohypertrophic muscular dystrophy.\textsuperscript{1, 5, 8} All components of the electrocardiogram can be affected. In this report, our patient was no exception as arrhythmias and conduction disturbances were present in all the tracings taken during the last few months of his illness.

The vectorcardiogram appears to be less reliable than the scalar electrocardiogram, both as the earliest and the most sensitive index of dystrophic heart disease.\textsuperscript{3} The type of QRS loop seen in our patient can be found in individuals with coronary artery disease and infarction of the ventricular septum or inferior wall. However, coronary arteriography ruled out occlusion of the main arterial trunks and of their large branches. Extensive destruction of the myocardial fibers could, however, result in a QRS loop configuration simulating that seen in patients with coronary occlusion.

In contrast to the wealth of electrocardiographic data on patients with cardiac dystrophy, few hemodynamic studies can be found in the literature.\textsuperscript{3, 10–14} Gailani and co-workers\textsuperscript{10} unmasked latent congestive failure in two patients with muscular dystrophy by recording elevated pressures in the right

Figure 5

Sinus node artery (reduced from $\times 150$). (A) The lumen is markedly narrowed by endothelial proliferation and widespread cystic degeneration. (B) Van Gieson's elastic tissue stain showing the location of the internal and external elastic laminae.
cardiac chamber. Other investigators\textsuperscript{12–14} found elevated pulmonary capillary pressure in this condition and interpreted this as an indication of left ventricular failure.

The patient herein described showed marked increase of the right and left ventricular end-diastolic and pulmonary capillary mean pressures. These data indicate severe decompensation of both ventricles, the rise in pulmonary arterial pressure being secondary to the failure of the left ventricle. As previously reported by others,\textsuperscript{13, 14} the pulmonary arteriolar resistance was normal and, thus, cannot be blamed for the elevated pressures in the pulmonary artery and in the right cardiac chambers.

The cardiac output and index were found to be normal or increased by some investigators,\textsuperscript{8, 10} but studies done on patients in frank decompensation\textsuperscript{18, 14} showed them to be diminished. This was confirmed in the present case.

A marked susceptibility to cardiac arrhythmias during catheter manipulation has been noted by some authors.\textsuperscript{8} This problem was not encountered here.

\textbf{Angiographic Studies}

Our interest in the opacification of the coronary vessels in this patient was prompted by a previous case report describing an unusual noninflammatory degeneration of the arteries supplying the sinus and atrioventricular nodes in a 19-year-old man afflicted with the same disease.\textsuperscript{23}

The outline of the main trunks of both coronary arteries was very smooth. A detailed study of the cineangiograms failed to reveal any obstruction or narrowing, segmental or generalized, along the course of the vessels visualized by the usual technic now available. The postmortem findings were in agreement with those of the coronary cinearteriogram. Varnauskas and associates\textsuperscript{24} have described a marked straightening and narrowing of the branches of both main coronary arteries in several patients with obscure cardiomyopathies, but this was not found in our case.

Because of the persistence of supraventricular arrhythmias in our patient, particular attention was brought to the examination of the right atrial branch and of its subdivision irrigating the sinoatrial node. On close study of injections recorded with a "zoom lens,"\textsuperscript{25} the cineangiograms showed an abrupt ending of this particular vessel which was then considered to be occluded. Serial sections of this node and of its artery did actually reveal a marked degree of narrowing of its lumen by intimal proliferation or cystic degeneration located between the two elastic luminae. It is probable that the column of dye mixed with blood was so reduced by then that it could not be recorded on the cineangiogram even with the degree of magnification provided by the zoom lens.

Thus, even though the correlation between cineangiograms and postmortem microscopic examination was not complete, the cinearteriogram was still able to indicate the presence of pathologic changes in an arterial branch of very small diameter but of great physiologic importance.

In 1962, James\textsuperscript{23} described a noninflammatory arteriopathy involving the nutrient arteries to the sinoatrial and atrioventricular nodes of a patient with progressive muscular dystrophy who had succumbed to severe disturbances of cardiac rhythm and conduction. The arteriopathy found in the present case seems to be identical to that of James' patient. The only difference lies in a more pronounced involvement of the sinoatrial node artery in our patient, while the lumen of the atrioventricular node nutrient artery was much more severely compromised in James' observation. This may account for the fact that only supraventricular arrhythmias were observed in our patient, while severe atrioventricular block followed these arrhythmias in the case he reported.

It is assumed that the degeneration of the smooth muscle fibers of these small arteries is similar in etiology to degeneration of striated fibers in the myocardium and skeletal muscle.\textsuperscript{23} The lack of a surrounding inflammatory reaction differentiates this process from the various arteritides. Thomson\textsuperscript{26} reported similar findings in a case of dystrophia myotonica.
Atrial flutter-fibrillation and various forms of intraventricular and atrioventricular block were present during the last 8 years of the patient's illness. The tunica media of the artery to the sinoatrial node was the seat of cystic degeneration, but its lumen was not considered to be seriously reduced. The arrhythmias were attributed to the striking changes involving the neuromyocardium of the node, namely a marked increase in the fibrous component and a severe reduction in its myocardium. The connections between node and atrial myocardium were also fibrosed.

James has pointed out that the changes seen in some small myocardial arteries in progressive muscular dystrophy resemble those observed in large vessels (aorta, main pulmonary artery) in Marfan's syndrome. But as in his patient, the large vessels of our patient were spared.

In both diseases, ocular abnormalities and musculoskeletal deformities are common, and in both diseases the victims frequently die suddenly. This brings up the question of interrelationship of these two conditions. In the present state of knowledge, it is not yet possible to answer this question.

References
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