The Physiologic and Clinical Similarity Between Primary Amyloid of the Heart and Constrictive Pericarditis

By Rolf M. Gunnar, M.D., Robert F. Dillon, M.D., Richard J. Wallyn, M.D. and Edward I. Elisberg, M.D.

When primary amyloid infiltrates the myocardium, there is a loss of distensibility and a resistance to contraction similar to that seen in constrictive pericarditis. The clinical similarity between these two entities has been noted previously on only a few occasions and only one previous case of amyloid has had catheterization studies. A case of amyloid of the heart is presented with catheterization studies and the reasons for the clinical and physiologic similarity to constrictive pericarditis are discussed.

The essential pathology of constrictive pericarditis is the partial replacement of the epicardium and superficial myocardial layers by inelastic fibrous tissue. This interferes with diastolic filling of the ventricles and is recorded during right ventricular catheterization as a high end-diastolic plateau. In addition, the encasing and infiltrating lesion interferes with contractility and thereby reduces, somewhat, the systolic pressure anticipated in relation to the high diastolic filling pressure. This results in a pressure pattern in which the end-diastolic pressure is often greater than one-third the systolic pressure: a finding which has been considered diagnostic by some authors. The early diastolic dip seen in the right ventricular curve is due to the "drag" effect of the fibrous exterior and its tendency to resist change and to reach the resting state more quickly. It is fairly sharply demarcated because of rapid filling caused by the high pressure within the auricle.

Recently it has been shown by Hertzel, Wood and Burchell that similar pressure patterns can be found in other conditions and in amyloid of the heart specifically. In 1950, Fisher had shown the inability of the amyloid heart to augment its diastolic volume. Clinically this was not a new concept, for Couter and Reichert and Findley and Adams had noted the clinical similarity in patients with amyloid infiltration of the heart and those with constrictive pericarditis. Though a direct comparison of the two conditions had not been made prior to these reports, many cases of amyloid of the heart, as reported, demonstrated high venous pressure, low pulse pressure, marked peripheral edema, nonspecific electrocardiographic changes and unresponsiveness to conventional cardiac therapy as occurs in constrictive pericarditis.

When amyloid infiltrates the myocardium, it would seem logical to assume that the same physiologic situations as seen in constrictive pericarditis occurs. The main difference would be that the constrictive element would now lie within the myocardium and hence, perhaps, interfere even more with the ejection force of the ventricle.

We have recently observed a case of "primary" amyloidosis with cardiac involvement that clinically and by catheterization study simulated constrictive pericarditis.

Case Report

E. R., a 49 year-old Negro woman, was admitted to Cook County Hospital Aug. 26, 1953, complaining of dyspnea, cough, ankle edema and abdominal pain. She had been well until November 1952, when she had an episode of right upper quadrant pain associated with some nausea and vomiting. This lasted about eight hours and a diagnosis of liver disease was made by her physician. She did fairly well until March 1953, when she began noticing swelling of the ankles and abdomen. The
ankle edema subsided with mercurials, but in July 1953 it recurred with increasing abdominal distention. At this time, the patient again had some “cramping” right upper quadrant pain. The edema persisted throughout the month prior to admission, despite mercurials. The patient developed a persistent, nonproductive cough a few days before admission and this was associated with exertional dyspnea. She denied orthopnea and paroxysmal nocturnal dyspnea, but at the time of admission seemed more comfortable while sitting up.

Her past history was negative for rheumatic fever, scarlet fever, heart disease and venereal disease. The patient had a very poor dietary history including no meat and very little bread. Systemic review revealed no sweats, fever, urinary difficulty or gastrointestinal complaints other than the right upper quadrant pain.

Physical examination revealed a chronically ill Negro woman, sitting up in bed in no acute distress. Blood pressure was 118/90, pulse 100, temperature 98 F., respiration 20 per minute. Her skin was dry. Pupils reacted to light and accommodation. The fundi were normal. The tongue was thought to be slightly larger than normal and somewhat reddened, but the patient stated it had been that way all her life. The neck veins were distended and pulsating. Examination of the chest showed flatness in the left base with decreased breath sounds. There were a few moist rales in both lung bases. The heart was enlarged to the anterior axillary line. The aortic second sound was equal to the pulmonic. The mitral first tone was accentuated and there was a protodiastolic gallop with a late diastolic rumble lasting up to the first tone. There was soft blowing apical systolic murmur. The liver was enlarged four fingerbreadths below the costal margin with a firm, sharp edge. There was shifting flank dullness. Pitting edema extended over the thighs and abdominal wall. Pretibial edema was of moderate severity. Pelvic and rectal examinations were normal. The reflexes were physiological.

On August 29, a thoracentesis yielded 1300 cc. of slightly cloudy, straw colored fluid from the left pleural cavity. Following this the patient was able to lie flat in bed comfortably. Specific gravity of the fluid was 1.013.

Laboratory Findings: Urine: Specific gravity was 1.010, albumin 2 plus, sugar absent, and microscopic examination negative. Blood count: hemoglobin was 80 per cent, white blood cells 7,700 with 60 neutrophils, 7 band forms, 2 basophils, 28 lymphocytes and 3 monocytes. The sedimentation rate was 30 mm. in 1 hour. Kahn was negative. Smears and cultures of the pleural fluid were negative. Three blood cultures were negative. Non protein nitrogen was 41 mg. per/100 cc., total protein 7.4 Gm. per 100 cc., the albumin globulin ration 4.1:3.3, cholesterol 164 mg. per 100 cc., alkaline phosphatase 4.3 B. U., icterus index 6 units, gamma globulin 2.61 Gm. per 100 cc., thymol turbidity 2.0 units and cephalin flocculation 2 plus.

Chest x-ray films on admission showed a left pleural effusion. After thoracentesis other x-ray films showed a small amount of fluid in the right base. The heart appeared only slightly larger than normal with no characteristic configuration (fig. 1). Fluoroscopic examination of the heart revealed left atrial (fig. 2) and left ventricular enlargement with very poor pulsations, particularly of the left ventricle. Electrocardiograms showed low voltage in all leads with inverted T waves in V1 through V4 and aV5, and flat T waves in aV6.

Hospital Course: The patient was placed on a low-salt diet and given mercurial diuretics and digitalis with very little response. Single daily temperatures were consistently normal. On September 1, another left thoracentesis yielded 900 cc. of straw colored fluid with specific gravity of 1.013. The patient maintained a gallop rhythm and the edema. A Mantoux was positive 1:10,000. On September 9, venous pressure was 320 mm. of saline, and circulation time (magnesium sulfate) 27 seconds. On Sept. 11, 1953, the patient was started on streptomycin and para-aminosalicylic acid (PAS) because of the possibility of a tuberculous pericarditis. On Sept. 23, 1953, the chlorides were 83 mEq per liter, sodium 129 mEq per liter and potassium 3.2 mEq per liter and the patient was put back on a general diet. In addition she was given oral potassium chloride. The pleural fluid recurred.

Fig. 1. Posteroanterior view of the chest after thoracentesis.
on the left and appeared on the right. Cardiac findings remained unchanged. About this time a purpuric skin lesion appeared on the anterior chest and neck which was considered to be a drug eruption by the dermatology consultants. The para-aminosalicylic acid was stopped and the patient was put on isoniazid.

By October 5, the nonprotein was 52 mg. per 100 cc., creatinine 3.4 mg. per 100 cc., chloride 93 mEq per liter, sodium 129 mEq. per liter, potassium 3.8 mEq. per liter. Because of lethargy, weakness and slight mental confusion the patient was given 300 cc. of 3 per cent saline intravenously with potassium chloride and oral fluids were restricted. The next day she was slightly improved but very weak. Blood pressure was 90/80, pulse 80. There was an increase in the purpuric skin lesion but the edema was unchanged. She was given an additional 300 cc. of 3 per cent saline and potassium chloride intravenously but expired early in the morning October 10, her forty-fifth hospital day.

Cardiac catheterization studies done on October 2 are shown in table 1 and figures 3 through 6 and will be discussed in relation to the postmortem findings.

Autopsy Findings: A specimen of skin was normal but unfortunately was not removed from the area of the purpuric lesion. The right pleural space contained 1500 cc. and the left 750 cc. of a clear, straw-colored fluid. The lungs were slightly edematous with some thickening of the hyperemic septa. The small branches of the pulmonary arteries revealed some intimal thickening.

The heart weighed 500 Gm. and the pericardial sac contained 10 cc. of a clear fluid. Both ventricles were enlarged but there was slight preponderance of the right ventricle. The epicardium appeared somewhat puckered but otherwise was free. Around the inferior vena cava at its entrance into the right atrium there were some fibrotic strands between the epicardium and extending slightly into the surrounding mediastinum. These adhesions caused slight kinking of the inferior vena cava which showed phlebosclerosis, but obviously were not contributory to the clinical picture since no similar obstruction to the inflow of the superior vena cava could be found. On section, these strands were apparently due to amyloid involvement of the pericardium. The myocardium of the right ventricles was thickened and the papillary muscles were flattened. The tricuspid valve was thickened irregularly but showed no anatomical evidence of dysfunction. The right atrium was dilated and thickened. The left atrium was dilated but its endocardium showed no thickening. The left ventricle was thick-walled and the papillary muscles were prominent. The mitral ring measured 8 cm. in diameter and the cusps were irregularly thickened throughout. The chordae tendineae were matted together and thickened. There was evidence of mitral stenosis and incompetence. Microscopic sections of the myocardium showed perivascular infiltration by a homogenous material which separated the muscle fibers. This did not stain with Congo red but stained metachromatic with methyl violet and was therefore atypical amyloid or para-amyloid. The deformity of the mitral valve was seen to be due to infiltration by a similar material.

The liver weighed 1800 Gm. and revealed severe passive congestion. The arteries showed extensive amyloid infiltration. The areas showing most marked amyloid showed more marked congestive changes. The spleen weighed 200 Gm. and showed marked amyloidosis of the arteries.

There was extensive amyloid infiltration of the skeletal muscles but not of the adrenals. The ovaries and thyroid showed amyloid infiltration. The kidneys showed lamellated casts especially in the distal convoluted tubules. These stained with Congo red and a similar material could be seen in the glomerular spaces. There was a cellular reaction around the casts and in some places epithelial giant cells were seen. This was considered to be a myeloma kidney.

Microscopic sections of the bone marrow showed accumulations of immature plasma cells which in many areas replaced the normal bone marrow elements. Lymph nodes also showed tumor like groups of typical myeloma cells.

The final anatomic diagnosis was diffuse myelo-
matosis; primary amyloidosis with involvement of liver, spleen, muscle and the myocardium and mitral valve (resulting in some degree of mitral stenosis and incompetence); myelomatous nephropathy; and cardiac failure.

**COMMENT**

Clinically observed venous engorgement was confirmed by the finding of marked right atrial hypertension (fig. 3). The atrial tracing shows a rounded elevation coincident with ventricular activity and lending somewhat of an “M” or “W” shaped configuration to the over-all contour. The principle negative deviation of the atrial pressure curve occurs prematurely in the isometric relaxation phase of the ventricle and is due to the rapid egress of blood from atrium to ventricle when the intraventricular pressure falls below the venous pressure.

The ventricular pressure curves obtained (fig. 4) in the presence of an extensive amyloid deposition is one of an inelastic and hypodynamic chamber. While the systolic peak exceeds

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**Fig. 3.** Right atrial pressure curve; pressures in mm. Hg.

**Fig. 5.** Pulmonary artery pressure curve; pressures in mm. Hg.

**Fig. 4.** Right ventricular pressure curve; pressures in mm. Hg.

**Fig. 6.** Radial artery pressure curve; pressures in mm. Hg.
the normal limit, it is less than that expected in relation to the high filling pressure. There is also an early diastolic dip. This dip and consequent rise to a "diastolic plateau" reflect rapid filling of the ventricle which is due, in addition to a high venous filling pressure, to limited distensibility of the ventricle. In this patient the resting right ventricular diastolic level exceeds one-half the systolic level.

The biventricular character of the process is reflected in an abnormally elevated pulmonary "wedge" pressure. The limitation of the left ventricle is further reflected in a low systemic pressure (fig. 6) which has a narrow systolic peak in its tracing. The low systemic pressure and small systemic arterial pulse wave indicate the limitations this condition has imposed upon effective stroke output.

The cardiac output at rest and on mild exercise is markedly decreased (table 1). The stroke volumes are about one-third of normal. These findings are indistinguishable from those of constrictive pericarditis.

The apical presystolic murmur and dilatation of the left atrium were undoubtedly due to the mitral stenosis secondary to amyloid infiltration. This could have contributed to the high capillary venous "wedge" pressure and limitation of cardiac output. It is impossible to distinguish this from the effect of the infiltration of the left ventricular myocardium, but the postmortem findings do not indicate enough anatomical change in the mitral valve to have caused this rise. Catheterization studies could only be interpreted as due to an encasing lesion involving both ventricles.

The diagnosis in this case could have been established by skin biopsy of the purpuric areas had this been done. The skin lesion and the large tongue should have suggested the diagnosis but these findings become more prominent in retrospect than at the time of examination. The auscultatory evidence of mitral stenosis could have been more easily explained on the basis of amyloidosis than constrictive pericarditis, since valve deformities have been described in primary amyloidosis. The interesting association of myelomatosis will be discussed elsewhere.

**Conclusion**

This case illustrates well the mechanical interference with cardiac function of amyloid infiltration of the myocardium. As in constrictive pericarditis, the diastolic volume is limited and, as the ventricle fills, the pressure rises suddenly to reach the end-diastolic pressure giving the early, diastolic "dip" and high plateau. The systolic pressure is not elevated proportionately because of interference with ventricular contraction. The resting right ventricular diastolic pressure exceeds one-half the systolic level, well within the limits described as diagnostic for constrictive pericarditis.

The clinical similarity is also striking since low peripheral pulse pressure, elevated venous pressure, unresponsiveness to therapy, relatively small heart with poor pulsations and marked ascites are prominent features of adhesive pericarditis. The purpuric rash was characteristic of amyloid of the skin as described by Goltz and may well have established the diagnosis ante mortem had a biopsy been done.

It would seem that any lesion which causes interference with diastolic expansion of the heart could produce intracardiac pressure patterns indistinguishable from those of constrictive-

**Table 1. Catheterization Data**

<table>
<thead>
<tr>
<th>Pressures, mm. Hg.</th>
<th>Right Atrium</th>
<th>Right Ventricle</th>
<th>Pulmonary Artery</th>
<th>Pulmonary &quot;Wedge&quot;</th>
<th>Radial Artery</th>
<th>Arterial Oxygen</th>
<th>Cardiac Output</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>Exercise</td>
<td>Rest</td>
<td>Exercise</td>
<td>Rest</td>
<td>Exercise</td>
<td>Rest</td>
</tr>
<tr>
<td>Right Atrium</td>
<td>25</td>
<td>28</td>
<td>43/28</td>
<td></td>
<td>46/29 (35)</td>
<td>50/36 (39)</td>
<td>92/61 (68)</td>
</tr>
<tr>
<td>Right Ventricle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>99%</td>
<td>98%</td>
<td>90</td>
</tr>
<tr>
<td>Pulmonary Artery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>179</td>
<td>224</td>
<td>180</td>
</tr>
<tr>
<td>Pulmonary &quot;Wedge&quot;</td>
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<td>Radial Artery</td>
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* B.S.A. = 1.6 M².
tive pericarditis. This might be localized in any layer of the heart, e.g. fibroelastosis of the endocardium, myocardial amyloidosis or fibrosis and pericardial constriction due to fibrosis or neoplasm. The effect of all these processes is the inhibition of the normal elastic and contractile responses of the muscle.

Summary

A case of primary amyloidosis involving the heart is presented. The similarity of the clinical and cardiodynamic findings of this entity to the findings present in constrictive pericarditis is emphasized, and the reason for this similarity, namely, the inelastic nature of the ventricle is discussed.

Sommario in Interlingua

Quando amiloide primari se infiltra a in le myocardio, il occure un perdita de distensibilitate et un resistentia al contraction que es simile a lo que es observe in pericarditis constrictive. Le similaritate clinic e iste condizione es evident in pauc casos, e studios de catheterisation ha solmente essite executate un vice unico. Le presente reporto concerne un caso de amyloide del corde in que studios de catheterisation eseva executate. Es discutite le reationes del similaritate clinic e physiologic de iste condition con pericarditis constrictive.

References

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