Clinical communications

Systemic amyloidosis presenting as constrictive pericarditis. A case studied with cardiac catheterization

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Primary systemic amyloidosis is a rare disorder that has been diagnosed *pre mortem* with difficulty. Yet in 51 fatal cases presented by Lindsay,[1] death was attributable in 22 to cardiac failure, and in 18 of these the amyloid involvement of the heart was responsible for this failure. Recently, it has been pointed out that systemic amyloidosis can present a clinical picture similar to that of constrictive pericarditis.[2-7] It appears that in some of the patients who present in congestive heart failure a diagnosis might be made *ante mortem* if this clinical similarity were remembered.

The following is the report of a case of primary systemic amyloidosis presenting as constrictive pericarditis and studied with the aid of right heart catheterization.

Case report

E.H.M. (UMH #934019) was a 49-year-old truck farmer who, in late February, 1959, passed a life insurance examination, demonstrating good exercise tolerance and a normal urinalysis. In May, he developed rapidly progressive exertional dyspnea which caused his hospitalization elsewhere with hepatomegaly. In June, he lost his taste for cigarettes, and noted increasing abdominal distention, swelling of the ankles, and trepopnea without orthopnea. Because of unresponsiveness to digitalis and diuretics he was admitted to the University of Michigan Hospital on Aug. 22, 1959.

On physical examination, he was slightly icteric, and lay flat in bed without discomfort, despite anasarca. His blood pressure was 90/70 mm. Hg, with a paradoxical pulse which measured 8 mm. The pulse rate was 92, and the respiratory rate was 14 per minute. There was marked distention of the neck veins even when he was in the sitting position, and evidence of bilateral pleural effusions. No râles were heard. The heart was enlarged to the left anterior axillary line, and the point of maximum impulse was absent. The heart sounds were of good quality, with an accentuated P_2 and a protodiastolic extrasound along the left sternal border. No murmurs were heard. The abdomen was markedly distended by ascites and a hard liver, which was enlarged to just below the iliac crest and umbilicus. There was 4+ edema of the scrotum, thighs, and ankles. The remainder of the examination was unremarkable.

The hemoglobin was 16.2 Gm. per 100 ml., with a hematocrit of 53 per cent; the erythrocyte sedimentation rate was 2 mm. per hour; the white blood cell count was 8,900 per cubic millimeter, with 77 mature polymorphonuclear leukocytes, 1 band form, 12 small lymphocytes, and 10 monocytes per hundred. The urinalysis was normal, except for an initial 4+ protein, which subsequently fell to trace. There was no Bence-Jones protein. The blood urea nitrogen was 37 mg. per 100 ml.; the alkaline phosphatase was 33.5 KA units, and total bilirubin was 3.6 with 1-minute direct of 1.6 mg. per 100 ml. Thymol turbidity, cephalin-cholesterol flocculation, and prothrombin concentration were normal. The total serum proteins were 6.5 Gm. per 100 ml., with an A/G ratio of 3.3, and an electrophoretic pattern that showed a slight increase in $alpha_2$ and beta globulins.

Cardiac fluoroscopy demonstrated cardiomegaly and decreased amplitude of pulsations. An electrocardiogram showed small QRS complexes and flat

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T waves. On September 1, catheterization of the right side of the heart was carried out. The ventricular systolic pressure reached a peak of 48 mm. Hg, or twice normal, followed by a sharp early "diastolic dip" to a low point of 17 mm., but abruptly thereafter the pressure rose to a plateau of 25 mm. and remained there throughout diastole. The ratio of the plateau pressure to the peak ventricular systolic pressure was 0.52 (Fig. 1). The right atrial pressure tracing reflected the fact that in diastole the atrium and ventricle form a common chamber. It demonstrated a parallel deep early "diastolic dip" that never fell to the base line and the rapid rise to a plateau. The subsequent smaller dip coincided with atrial diastole (Fig. 2), and completed the typical "M" pattern once thought to be characteristic of constrictive pericarditis.

The sternal marrow was characterized by an erythroid hyperplasia, as well as an increase in the plasma cells to 16 per cent. Many of these appeared to be abnormal, but none were considered to be malignant. A gum biopsy, carried out a few days before death, demonstrated extensive infiltration of the walls of the blood vessels by amyloid.

Throughout his hospital course the patient remained totally resistant to all diuretic measures and died, still lying flat in bed, on Sept. 6, 1959. The clinical diagnosis was systemic amyloidosis with plasmacytosis.

The postmortem examination disclosed bilateral pleural effusions, pulmonary congestion, hepatomegaly, and ascites. The major abnormality centered about the heart, which weighed 535 grams. The thickness of the left and right ventricular walls was 13 and 5 mm., respectively. There were no pericardial adhesions, but 140 ml. of clear pericardial fluid. The myocardium appeared pale, pink, and slightly shiny. It was firm and retained its shape after section.

Microscopically, there was generalized amyloid infiltration of virtually all organs, with particularly marked involvement of the heart, liver, lungs, adrenal glands, and spleen. The skeletal muscles and blood vessels were similarly involved. Grossly, the pulmonary vasculature was normal, but on microscopic examination there was extensive involvement by amyloid. The kidneys were only minimally involved. A more detailed examination of the heart demonstrated a normal pericardium. There was a patchy but generalized distribution of amyloid material in valve cusps, leaflets, and blood vessels, as well as interstitial infiltration of the myocardium. Myofibrils in the more involved areas demonstrated atrophy and fragmentation, whereas other, less involved myofibers were hypertrophic. An interesting but not unusual[8] finding in the marrow was the presence of multiple microscopic foci composed essentially of pure cultures of plasma cells. Some of these cells were enlarged and binucleated. The pathologist, therefore, concluded that this patient had multiple myeloma with paramyloidosis rather than amyloidosis with plasmacytosis.

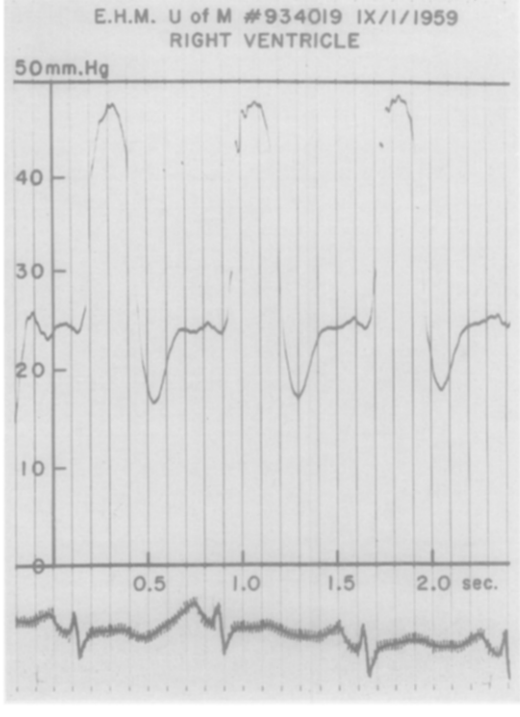

Fig. 1. The patient's right ventricular pressure tracing (*upper curve*) and Lead II of his electrocardiogram (*lower curve*).

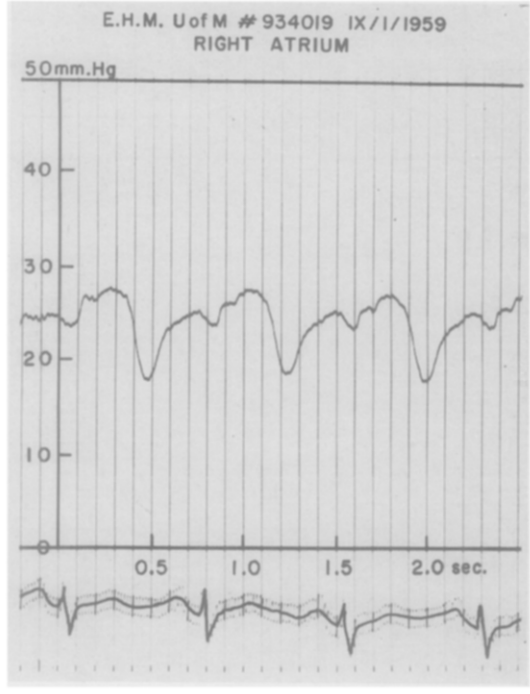

Fig. 2. The patient's right atrial pressure tracing (*upper curve*) and Lead II of his electrocardiogram (*lower curve*).

Discussion

This case presented several interesting points to the clinician. The first was the establishment of the diagnosis of amyloidosis. It was believed that severe failure of the right side of the heart might be a feature of a disease with multisystem involvement. The presence of plasmacytosis (or multiple myeloma) suggested either amyloidosis or paramyloidosis. This was confirmed by gum biopsy.

Differentiation between multiple myeloma with paramyloidosis and amyloidosis with plasmacytosis is difficult, but the latter diagnosis was favored because of the benign appearance of the plasma cells.

A third and thought-provoking facet was the resistance of the failing amyloid heart to intensive therapy.

The last interesting feature of this case is its similarity to constrictive pericarditis. In pericarditis the fibrosing process involves both the right and left sides of the heart and, quite reasonably, restricts the usual ventricular distensibility. This restriction is reflected in a rather characteristic pressure pulse tracing on right heart catheterization, first described by Bloomfield and associates[9] and subsequently studied and further defined by others.[10-13] Briefly, the changes include an early diastolic dip in the ventricular pressure, which does not fall to normal values, and a rapid rise to a sustained elevated end-diastolic plateau. The subsequent systolic peak pressure is often elevated. However, the ratio of the pressure of the diastolic plateau to the ventricular systolic peak is characteristically greater than 0.3. The diastolic right atrial pressures generally reflect the changes which are occurring in the right ventricle, and thus demonstrate an increased mean pressure and a series of dips which give the tracing an "M or W" appearance.

That pericardial calcification alone, and even the fully developed clinical picture of constrictive pericarditis, need not be associated with the characteristic right-sided pressure pulse tracings was pointed out by Harvey and associates[14] and Lin and Anache,[6] respectively. On the other hand, it has been shown that several other pathologic entities can give a picture quite similar to that of constrictive pericarditis, both clinically and on catheterization of the right side of the heart. In 1946, Bloomfield and associates[9] noted that severe right-sided heart failure could produce similar tracings. This finding was substantiated by Wilson and associates,[13] who added acute pericardial effusion to the growing list. Myocardial fibrosis due to coronary atherosclerosis,[15] nonspecific myocarditis,[16] subendocardial fibrosis,[17] and cardiac hemochromatosis,[18] as well as limitation of ventricular distensibility due to *pectus excavatum*[19] have all been reported to produce right-sided pressure pulse tracings identical to those of classic constrictive pericarditis. Balchum and associates[16] went even further and suggested several entities that reasonably could be expected to give similar tracings. Among these are myocardial fibrosis associated with scleroderma heart disease and certain neurological entities, glycogen storage disease, and fatty or neoplastic infiltration. It is apparent, therefore, that the pressure pulse tracings obtained in constrictive pericarditis are not pathognomonic.

This lack of specificity seems to be quite logical when one considers amyloidosis in more detail. The extensive diffuse or nodular interstitial deposition of amyloid in the myocardium, as well as the infiltration of the endocardium and pericardium by this rather rigid material,[20] cannot but cause a decrease in the normal excursions of the ventricular chambers. The result[3] is an abnormal physiology similar to that described by Lyons and Burwell[21] for constrictive pericarditis. Specifically, right heart catheterization studies in this patient demonstrate changes in pressure which are identical to those described in chronic constrictive pericarditis. The same is true for the three previously reported cases of amyloidosis with cardiac involvement that have been studied with right heart catheterization.[4,5,7] In cardiac amyloidosis, as the right ventricle enters early diastole, the blood rushes under an increased pressure into the inelastic ventricular chamber. Because the ventricle is unable to dilate sufficiently, the pressure in this chamber never falls to less than 5 mm. Hg (Fig. 1), and instead again rises rapidly until the pressures in the two chambers and the

venous system are equalized at an elevated sustained end-diastolic plateau. The result is the early "diastolic dip" and plateau seen also in the tracings from patients with constrictive pericarditis. These changes in diastolic pressure are reflected in the atrial pressure tracings (Fig. 2). On auscultation, this sudden change in pressures produces the protodiastolic extra sound noted also in this patient. On the other hand, the right ventricular pressure in the normal person remains below 5 mm. Hg throughout this period because the ventricle is able to dilate (Fig. 3). During ventricular systole the peak pressure reaches 48 mm. Hg and is a reflection of pulmonary hypertension. In this case it is possibly due not only to inflow stasis on the left side of the heart because of amyloid restriction, but also to amyloid deposition in the pulmonary arterioles. Although Yu and associates[12] have considered a ratio of the end-diastolic to peak right ventricular pressure greater than 0.3 to be diagnostic of constrictive pericarditis, in this patient it was 0.52.

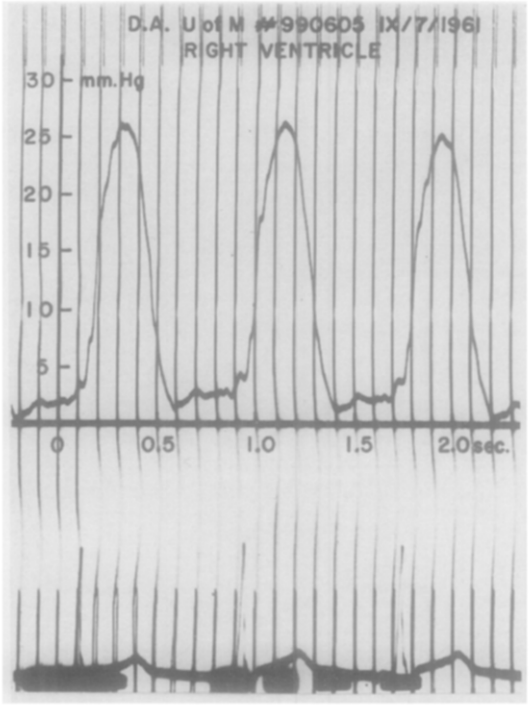

Fig. 3. A normal person's right ventricular pressure tracing (*upper curve*) and Lead II of his electrocardiogram (*lower curve*). Note the difference in the pressure scale.

It is clear, therefore, that the reported changes in right ventricular pressure in amyloidosis with cardiac involvement are indistinguishable from those seen in chronic constrictive pericarditis. Amyloidosis must then be considered in the differential diagnosis in patients who present with a clinical picture of constrictive pericarditis.

Summary

A case of systemic amyloidosis and plasmacytosis is presented. Both on clinical observation and cardiac catheterization, the features of this case simulated those of constrictive pericarditis. The pertinent literature is reviewed.

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