Primary Systemic Amyloidosis Mimicking Chronic Constrictive Pericardial Disease

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The characteristically altered physiologic pattern in chronic constrictive pericarditis is the result of the diminished cardiac expansibility. A widespread infiltrative myocardial disease in which cardiac expansibility was equally limited should simulate the former entity very closely. This extremely rare entity is illustrated in this case report.

PRIMARY amyloidosis is a rare disease; less than 60 cases have been reported to date. Lindsay surveyed the cardiac complications of 45 cases of primary amyloidosis and found that 30 had cardiac amyloid deposition and that 23 had signs of congestive failure. He believed that in some, the extensive amyloid deposition might have interfered greatly with the normal range of cardiac contraction and relaxation but none of the 45 cases were reported as simulating chronic constrictive pericarditis.

Chronic constrictive pericarditis is a relatively common disease. It is usually recognized late in its course after the reduced cardiac output has resulted in a pathognomonic physiologic complex. In this entity, the restriction of cardiac movement is caused by a thickened and sometimes calcified pericardium that may or may not be associated with a collection of pericardial fluid. A generalized myocardial disease would be capable of producing an identical symptom complex if the disease process could produce significant restriction of cardiac contraction and relaxation.

The stimulation of chronic constrictive pericardial disease by a generalized infiltrative myocardial disease is extremely rare; only one other case has been reported. In the case report to be presented all of the classic symptoms and clinical signs of constrictive pericarditis were superimposed upon the clinical manifestations of primary systemic amyloidosis.

CASE REPORT

The patient was a 38 year old white housewife, whose general health had been good prior to September 1948. Two pregnancies fourteen and eight years previously had been without untoward incident. In September 1948 she developed a "cold," characterized by excessive lacrimation, rhinorrhea, and headache. Approximately one week later she noted the onset of a pressing pain over the lower sternal synchronous with her heartbeat and intensified by exercise. This discomfort persisted continuously for one month and then shifted to the lower abdomen where it was augmented after eating.

She was admitted to a neighboring hospital November 21, 1948 complaining chiefly of fatigue, anorexia, and abdominal pain. In addition, echymoses had appeared in the soft tissues around the right eye without antecedent trauma. The remainder of the history was noncontributory. Significant physical findings were a blood pressure of 110/68, a persistent tachycardia of 130 per minute at bed rest, pallor, a small ecchymotic area around the right eye, and a few small petechiae under the tip of the tongue. Laboratory values were normal for the following procedures: reticulocyte and blood platelet count, bleeding, clotting, and clot retraction time, hematoctrit, blood glucose, blood nonprotein nitrogen, serum albumen, globulin, potassium, and sodium, urea clearance, basal metabolic rate, thymol turbidity and flocculation, cephalin-cholesterol flocculation, and repeated blood cultures. A Rumpel-Leede test was normal. X-ray examination of the upper gastrointestinal tract, kidneys, and colon as well as gastric analysis and biliary drainage were normal. The hemoglobin was 13.3 Gm. per 100 cc. and the erythrocyte count 3,940,000 per cubic millimeter. The leukocyte count was 11,700 per cu. mm., with a normal differential leukocyte count. The sternal marrow was moderately hypoplastic. A urinalysis was normal with the exception of a plus 3 proteinuria without Bence-Jones proteinuria. The stool showed a plus 4 guaiac reaction. There was 10 per cent retention of bromsulfalein at 45 minutes following the injection of 5 mg. per kilogram of body weight. The electrocardiogram revealed small complexes in Leads I, II and III with inversion of the T waves in Leads
II and III. The patient remained afebrile during her three weeks' hospitalization and was treated symptomatically.

Following discharge she continued to do poorly although her abdominal discomfort decreased somewhat in intensity. In January 1949 she was again hospitalized because of the passage of "one pint of fresh blood" from the rectum. Physical examination at this time revealed that ecchymoses of the buccal mucous membranes had appeared, the liver edge was palpable for the first time, and the reclining blood pressure was 82/52. The admission hemoglobin was 10.6 Gm. per 100 cubic centimeters. The leukocyte count was 6850 with a normal differential. Repeated determinations of the blood nonprotein nitrogen, and serum potassium, sodium, albumen, and globulin were normal. A Kepler water balance test was negative. A plus 4 guaiac reaction was again present in the stool. X-ray examination of the skull, colon, and chest was normal. Proteinuria persisted and the retention of bromsulfalein had risen to 22 per cent at the end of 45 minutes. The sternal marrow was hypoplastic with a shift of the myeloid-erythroid ratios from an initial 6:1 to 11:1. She was discharged after two blood transfusions and symptomatic therapy which was followed by gradual improvement although the hypotension and the tachycardia persisted.

In February 1949 she first noted oliguria and dependent edema and was admitted to the neighboring hospital for the third time on March 23, 1949. She appeared severely ill, was pale, and showed evidence of recent weight loss. The reclining blood pressure was 60/45 in the upper extremities and unobtainable in the lower; she complained of dizziness and lightheadedness in the upright position. Marked dependent edema was present and the liver edge was palpable at the level of the umbilicus. Proteinuria was again present; the microscopic examination of the urine revealed many leukocytes and a few erythrocytes per high power field with many fine granular casts per low power field. The hemoglobin was 11.5 Gm., the erythrocyte count 4,380,000, and the leukocyte count 6000.

She was admitted to the University Hospital March 26, 1949, approximately seven months after the onset of the first symptoms. Physical findings were as those previously described. The reclining blood pressure was 80/60, and the pulse rate 108 per minute with a significant pulsus paradoxicus. The facies was mask-like with some peri-orbital edema. The neck and other peripheral veins were markedly distended; sacral and peripheral edema of the lower extremities as well as signs of bilateral pleural effusion were present. A tender liver edge was palpable 10 cm. below the right costal margin. The left border of cardiac dulness was at the mid-clavicular line in the fifth intercostal space. The heart sounds were distant and regular. A prominent third sound was present in early diastole at the apex.

Bleeding, clotting, and clot-retraction time, prothrombin concentration, direct and indirect bilirubin, hemoglobin, erythrocyte and leukocyte counts, and the differential leukocyte count were normal. Urinalysis showed proteinuria and cylindria and urine cultures grew Staphylococcus aureus and a nonhemolytic streptococcus. The urea clearance was 64 per cent at the first hour and 59 per cent at the second. The blood urea nitrogen was 28.6 mg. per 100 cc. with an initial nonprotein nitrogen of 37 mg. per 100 cc.; this latter value subsequently rose to 82 mg. per 100 cc. The total serum proteins were 5.8 Gm. per 100 cc. with albumen 2.4 Gm. and globulin 3.4 Gm. per 100 cc. The cephalin-cholesterol flocculation test was negative at 24 and plus 3 at 48 hours. There was 32 per cent retention of bromsulfalein at 45 minutes (5 mg. per kilogram). Blood creatinine was 1.4 mg. per 100 cc. The arm-to-tongue circulation time was 35 seconds (normal 18 seconds). An old tuberculin series was negative for dilutions of 1/10,000 and 1/1000 and the Kahn serologic test was negative. Venous pressure in the right arm was 268 mm. of water. Electrocardiograms with standard limb leads, unipolar limb leads, and unipolar precordial leads were not remarkable except for the small QRS complexes and the flat T waves in all leads (fig. 1). Fluoroscopy demonstrated the heart to be of normal size; no pulsations of the cardiac silhouette could be definitely identified.

In view of the clinical and laboratory findings associated with the syndrome of constrictive peri-
cardial disease and the history of a hemorrhagic tendency, the possibility of a partially organized hemorrhagic pericardial effusion was considered and a diagnostic pericardial tap performed. Eighty-five cc. of rapidly clotting serosanguinous fluid was easily obtained and 50 cc. of air replaced. An x-ray film of the chest demonstrated the presence of additional significant pericardial fluid. Examination of the aspirated pericardial fluid failed to demonstrate acid-fast or other bacteria or neoplastic elements.

In spite of supportive therapy, the anasarca increased, periods of mental confusion became more frequent, and a shock-like state consistently occurred when the patient assumed the sitting position. In view of the possibility of some type of restricting cardiac disease an exploratory thoracotomy was performed April 4, 1949. During that procedure 275 cc. of serosanguinous fluid was removed from the pericardial sac. However, the pericardium itself appeared grossly normal. The right auricular appendage was distented, bluish, and definitely indurated. A partial pericardiectomy was performed and the pericardial space left in free communication with the left pleural cavity. Venous pressures were 240 mm. H₂O immediately before and after the operation and 300 mm. during the operation. On the second postoperative day the venous pressure was 300 mm. of water. Post-operatively her condition remained poor and death ensued on the eleventh hospital day.

Postmortem examination.—Autopsy with the exception of the head was performed six and one-half hours after death. The abdominal cavity contained 200 cc. of a straw-colored fluid; there were 700 cc. of a similar fluid in the right and 400 cc. in the left pleural cavity. The heart weighed 430 grams. The remaining pericardium was somewhat thickened but smooth. The epicardial surface underlying the surgical defect was slightly granular and greyish purple. The left ventricular wall measured 17 mm. and the right 4 mm. in thickness. The right auricle was markedly dilated; the left ventricle was also dilated to a moderate degree. An old thrombus was present in the right auricular appendage. The heart valves were normal. The right lung weighed 500 grams and the left 450 grams. The pleural surfaces were smooth. Cut sections of the lung revealed considerable edema fluid. There was slight congestion in the small intestine. The pancreas weighed 100 grams. The liver weighed 2000 grams. The right adrenal gland weighed 11 and the left 14 grams. The right kidney weighed 210 and the left 260 grams. A left para-ovarian cyst was present.

Sections were stained with methyl violet in addition to the usual stains. There was massive amyloid deposition in all organs with predilection of involvement of the walls of the small and medium-sized blood vessels.

In the heart there was acute fibrinous epicarditis with serous atrophy of the sub-epicardial fat and sub-epicardial hemorrhage. The nerves and blood vessels in the subepicardium revealed considerable amyloidosis, which in the blood vessels was deposited outside the endothelium. A few amyloid deposits in the adipose tissue did not appear to be related to blood vessels. Throughout the myocardium every muscle fiber appeared to be surrounded by amyloid material (fig. 2) with both atrophy and hypertrophy of the myocardial fibers. In addition there were manifold areas of necrobiosis with karyorrhexis, karyolysis, and vacuolation. Beneath the epicardium in the walls of the small to medium-sized blood vessels and in the substance of the cardiac valves were larger irregular hyalin masses. In some cases the hyalin material was located only in the media of the arteries. These larger masses of hyalin material and the smaller masses in the blood vessels gave a poor metachromatic reaction when stained with methyl violet. The right auricular appendage contained a large recent bland thrombus showing focal areas of beginning autolytic softening and organization. The nerve trunks and ganglia adjacent to the aorta contained amyloid deposition.

Fig. 2.—Section of the myocardium showing extensive involvement with amyloid with unit encasement of the individual fibers.
Discussion

In this case of primary systemic amyloidosis all of the clinical signs and symptoms of chronic constrictive pericarditis were present. The heart size was within normal limits, although the venous pressure on all occasions was over 250 mm. of water. Small QRS complexes and flat T waves were present in all electrocardiographic leads. No murmurs were audible and the heart sounds were quiet and regular. A prominent apical third heart sound was present in early diastole. The circulation time was prolonged. The systolic blood pressure ranged from 60 to 80 mm. Hg with a small pulse pressure. A persistent tachycardia and a significant pulsus paradoxus were present. The patient was not orthopneic although ascites, dependent edema, and bilateral hydrothorax were prominent.

It is unlikely that cardiac tamponade was a factor in the progressive cardiac embarrassment demonstrated in this case for the venous pressure remained elevated following the removal of all possible constricting structures. The myocardium was widely infiltrated with amyloid to the extent that all the individual fibers were encased in the material. The myocardium had lost its capacity for contraction and relaxation to the degree that cardiac diastole and systole were so restricted that the syndrome of chronic constrictive pericarditis was simulated physiologically.

Summary

A case is reported of primary amyloidosis with extensive myocardial deposition and simulation of chronic constrictive pericarditis.

Acknowledgments

We are indebted to Dr. Raymond Monto of Detroit for the information relative to the patient prior to hospitalization at the University Hospital and to Dr. J. Marion Bryant of Ann Arbor for his many helpful suggestions.

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Circulation. 1950;2:441-444
doi: 10.1161/01.CIR.2.3.441

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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