Congestive Heart Failure of Unusual Cause Affecting a Young Woman; Sudden Death

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CHAIRMAN: Today's case is a difficult one. Following presentation of the abstract, the case will be discussed by Dr. Roy W. Scott.

Abstract of Case. A.S., a 28 year old nulliparous Negro housewife was admitted for the seventh time to the Medical Service of Cleveland City Hospital on March 29, 1949, with the complaint of severe, progressive dyspnea of three days' duration. She died on the third hospital day.

The patient was first hospitalized at age 14 (1935) because of gonococcal urethritis and cervicitis. At this time the heart was normal. During this hospitalization the patient developed transient pain and tenderness in the right temporomandibular joint. Concurrently a small ulcer and a condyloma appeared on the left labium minus near the anus. Dark field preparations were positive for Treponema pallidum, and the blood Wassermann reaction was negative. Healing of the lesions followed a series of 14 intravenous injections of Mapharsen and a course of bismuth. She was readmitted for five days one month following discharge, because of pain and swelling of the right knee joint. These abated after symptomatic management.

The third and fourth admissions were at age 24 (1945), when she received 3,000,000 units of penicillin for recurrent gonococcal urethritis and cervicitis, as well as for positive blood and spinal fluid Wassermann reactions.

In December of 1948, at age 27, she was hospitalized for the fifth time because of cough productive of mucoid sputum of six months' duration, preceded by a sore throat. There had been night sweats, exertional dyspnea and paroxysms of nocturnal dyspnea for one month. During this period the patient noted transient, nondonscript precordial pain which was never anginal in character. Nine days prior to admission there developed orthopnea and ankle edema. There had been no weight loss, diarrhea, nervousness or heat intolerance. This hospitalization lasted until discharge on Jan. 5, 1949.

Physical Examination. The temperature was 38 C., respiratory rate 24, blood pressure 130/90, and the vital capacity 1300 cc. (56 per cent of normal). The ocular fundi were normal. Examination of the heart revealed a diffuse apical impulse without increased activity. The left border of cardiac dullness was in the sixth intercostal space 9.5 cm. from the midmural line, and the right border 1.5 cm. from the right sternal border in the fourth intercostal space. The mechanism was sinus with a diastolic gallop rhythm. The heart sounds were of poor quality, the second pulmonic being louder than the second aortic sound. At the apex there was a moderately harsh, low pitched holosystolic murmur, transmitted well into the axilla. A softer, higher pitched systolic murmur was localized to the second right parasternal area. There were no thrills and the area of upper retromanubrial dullness was not widened. All peripheral pulses were equally and bilaterally palpable and the vessels were soft and pliable. A pulsus alternans was felt in the radial artery. The jugular veins were distended (venous pressure: 230 mm. of saline). Moist rales were present at both bases, the liver edge was palpable and tender several centimeters below the right costal margin. There was slight pitting edema over both ankles.

Laboratory Findings. The hemoglobin was 12 Gm., the red blood cell count 5,100,000, the white blood cell count 13,300 with 93 per cent polymorphonuclear leukocytes. The erythrocyte sedimentation rate was 18 mm. in one hour (Wintrobe). Urinalysis was normal, except that the specific gravity of the urine was never greater than 1.024 even after 18 hours of fluid abstinence. The blood and spinal fluid Wassermann reactions were positive; there were 30 mg. of protein in the spinal fluid, with 10 mononuclear cells and a first zone gum stactic curve. Values for fasting blood sugar, blood urea nitrogen and serum proteins were normal. Cardiac fluoroscopy (following digitalization) revealed moderate generalized cardiac...
enlargement. The circulation times determined with ether and Decholin were 17 and 37 seconds, respectively. The admission electrocardiogram was not abnormal.

**Hospital Course.** Congestive failure was controlled promptly with digitals, mercurial diuretics and a salt poor diet. No growth was obtained from 13 blood cultures drawn during the first five hospital days. Hemolytic aureus and albus staphylococci were grown from two other cultures but were considered contaminants. Nevertheless, on the sixth hospital day the intramuscular administration of aqueous penicillin was begun, and continued for 21 days for a total dosage of 9,600,000 units. Two curiour teeth were removed during this time. The temperature, which varied between 37 and 38.5 C., though gradually defervescing, failed to return to normal by the end of hospitalization, although the white blood cell and differential counts did so. The heart rate varied between 50 and 110 beats. In 12 random determinations, the blood pressure varied between 150 and 114 systolic, and 120 and 80 diastolic. Serial electrocardiograms revealed gradual and progressive inversion of T wave in leads II and III, slurring of QRS in lead III, and reduction in voltage of R in the left precordial leads. The patient was discharged to the out-clinic on the thirty-second hospital day.

Two weeks later the patient was re-admitted for the sixth time because of chills, fever and dull pain in both lower hemithoraces with flank radiation of three days' duration. *Escherichia coli* was cultured from two catheterized specimens of urine, and one blood culture was negative. At this time there was no clinical evidence of heart failure, although a six-foot roentgenogram of the chest revealed that the heart was still slightly enlarged. The rhythm was sinus without gallop. The heart sounds were of fair quality and no murmurs were heard. The urinary tract infection responded to sulfadiazone administration, and the patient was discharged after two weeks.

**Final Admission**

The patient was again admitted on March 29, 1949. Three weeks before this terminal hospitalization the patient noted the onset of warmth and tenderness in the left calf, and three days before admission she became suddenly and progressively more dyspneic. There was no chest pain or hemoptysis.

**Physical Examination.** The temperature was 39 C., the blood pressure was 140/110, the heart rate was 140, and the respiratory rate 40 per minute. The patient was dyspneic, orthopneic, apprehensive and restless. The pupils were round, regular, equal and responded to light and in accommodation. There were grade 1 changes in the arterioles of the fundi. The jugular veins were markedly distended with the patient in the upright position. The hemithoraces were symmetric and the respiratory movements rapid and shallow. A few fine rales were heard at the left base; the breath sounds were slightly depressed at the right base. There was an increase in palpable activity over both ventricles. The point of maximal impulse encroached upon the sixth intercostal space in the anterior axillary line. The second pulmonic sound was now much louder than the second aortic sound, and was reduplicated. There was a sinus mechanism and a diastolic gallop rhythm was present. A loud, harsh systolic murmur was present at the apex and was well transmitted to the axilla. The liver edge was not felt, but there was tenderness over the right upper abdominal quadrant. There was increased warmth of the left calf, which was swollen and tender, and Homan's sign was present. There was also tenderness over the posterior aspect of the right leg and thigh.

**Laboratory Data.** The urine had a specific gravity of 1.014 with 4 plus albuminuria, but was otherwise negative. The hemoglobin was 13 Gm., red blood cell count 4,500,000, white blood cell count 11,500 with 72 per cent polymorphonuclear leukocytes, 17 per cent lymphocytes, 10 per cent monocytes and 1 eosinophil. The blood urea nitrogen was 13.0 mg. per 100 cc., and the fasting blood sugar 125 mg. per 100 cc. An electrocardiogram revealed low voltage T waves in lead I, inverted T waves in leads II, III, CF₄, CF₅ and CF₆, small Q waves in lead III and elevated S-T segments in leads III and CF₅, and depressed S-T segments in leads I and II.

**Hospital Course.** The patient was given oxygen by nasal catheter, aqueous penicillin, and heparin and Dicumarol. Thirty six hours later the blood pressure suddenly dropped and the patient died shortly in spite of all therapeutic efforts.

**DR. ROY W. SCOTT:** It is apparent from reading this protocol that the pathologist has selected an unusually interesting case. I shall give a synopsis of what I consider to be the pertinent features. The first several admissions deal with something of a venereal odyssey. At the tender age of 14 this patient had both gonorrhea and syphilis. Ten years later she had some more difficulty with these same diseases and at this time it was found that her blood and spinal fluid Wassermann reactions were strongly positive. The role that syphilis may have played will be discussed later.

One month after her release in 1935 pain and tenderness appeared in the right knee. I don't believe this was gonorrheal arthritis, since it responded rapidly to symptomatic therapy. It certainly does not sound like rheumatic arthritis, because rheumatic fever,
as far as the joints are concerned, is usually a migratory and not a monoarticular arthritis.

In December of 1948, about four months before her death at the age of 27, she was again hospitalized. From there on, until the terminal episode, we have a very classic picture of congestive failure, both subjectively and objectively. She had paroxysmal nocturnal dyspnea, effort dyspnea and orthopnea, and on examination there was a gallop rhythm and a pulsat alternans, both grave signs of myocardial distress, whatever the cause. There was an apical systolic murmur, transmitted to the axilla, which was still present at the end of her hospital stay, but which was not heard on the next to the last admission, so I assume that the murmur was due to ring dilatation rather than organic mitral valvular distortion. There was obvious congestive failure.

Now, the rather remarkable thing, to me, is that with treatment for about a month, she apparently cleared sufficiently so that the Staff felt justified in discharging her.

In the next admission she had what appeared to have been an acute infection of her kidneys. She had fever, leukocytosis and responded to sulfadiazine. At the time of this admission, you will note that the rhythm was regular, and neither a gallop nor a murmur was heard, so that the cardiac murmurs she had at the time she was decompensated completely cleared.

The terminal episode, three days before death, I feel reasonably certain was due to pulmonary embolization, since we have a clear clinical picture, including the electrocardiographic deformities characteristic of acute cor pulmonale, seen in patients with massive pulmonary emboli.

To return now to the most difficult part in this protocol, namely, the cause of the bout of congestive failure some three months before death. You recall that with treatment the congestion cleared, the gallop rhythm and pulsat alternans disappeared, no murmurs were heard, and the heart size returned to near normal. The commonest cause of heart failure in patients below the age of 30, namely, rheumatic heart disease, merits consideration, but one finds little here to support such a diagnosis. There was no clear evidence of valve disease, and the course pursued by the patient was not that of an overwhelming rheumatic myocarditis. The presence of gallop rhythm, pulsat alternans, and cardiac dilatation point to a damaged myocardium. One might postulate that the penicillin administered in 1945 for syphilis might have arrested a subacute bacterial endocarditis. The possibility always exists that, though not heard on the next to the last admission, the mitral murmur may have been organic. The 1948 attack of congestive failure may have resulted from focal damage to the myocardium frequently found in arrested cases of subacute bacterial endocarditis dying of heart failure. However there was no clinical evidence of a malformed heart or of a scarred endocardium, so that this possibility seems unlikely.

Another rare disease of undetermined etiology affecting the myocardium and sparing the endocardium and pericardium, interstitial or Fiedler's myocarditis, must be mentioned. In the few cases reported, fever has been persistent, and, once congestive failure appears, death ensues in spite of treatment. Therefore, I doubt that this is a case of Fiedler's myocarditis.

Since this patient was known to have had syphilis for some years before death, and since the aorta is so often involved in late syphilis, we may be dealing with extensive fibrotic lesions in the myocardium, secondary to coronary ostial occlusion? Marked narrowing or complete occlusion of the ostia from syphilis often causes anginal symptoms and the patients die suddenly without the picture of congestive failure.

So in conclusion, it is my opinion that we deal here primarily with myocardial disease secondary to coronary disease, as rare as this is in young Negro females. In this conclusion, I may be unduly prejudiced by a case we observed here some years ago. A Negro female, aged 20, was admitted in frank congestive failure of one month's duration. There was no history of rheumatic fever and the blood Wassermann reaction was negative. X-ray study showed the heart to be definitely enlarged, particularly in the region of the left
ventricle, and a gallop rhythm and pulsus alternans were present. Except for a grade 3 apical systolic murmur, the heart sounds were not remarkable. With treatment, compensation was restored, the systolic murmur, gallop rhythm and pulsus alternans disappeared. The patient was discharged without any etiologic diagnosis having been established. Two months later, she was readmitted again in congestive failure. The heart shadow was slightly larger, a gallop rhythm and pulsus alternans were present as well as the apical systolic murmur. Two months later, in spite of having previously responded to treatment, she failed to do so and succumbed.

Death was due to myocardial failure, but no etiologic diagnosis was made. At post-mortem examination, there was found extensive proliferative endarteritis of the coronary arteries, with definite necrosis and fibrosis of the myocardium. The clinical course pursued by this patient, although not identical with the one under consideration here, was similar in so many respects, that I hazard a guess that the pathological findings may be similar.

CHAIRMAN: Thank you, Dr. Scott. Can you help Dr. Scott with your x-ray observations, Dr. Hauser?

DR. HARRY HAUSER: We will present the pertinent films. A chest film taken in March 1945, shows heart and aorta of normal configuration, whereas a cardiac fluoroscopy done on Dec. 8, 1948, shows a mild degree of cardiac enlargement. Another film taken in January of 1949 shows no change. A chest film was unfortunately not obtained during her terminal hospitalization.

Dr. Scott's Diagnosis

1. Organic heart disease, probably coronary sclerosis and fibrosis, with proliferative endarteritis.

![Fig. 1. Right ventricle and interventricular septum with organizing mural thrombus in lower ventricular and apical region.](http://circ.ahajournals.org/DownloadedFrom)
CONGESTIVE HEART FAILURE OF UNUSUAL CAUSE


Clinical Diagnosis

1. Shock, etiology undetermined, probably secondary to thrombophlebitis of left leg with pulmonary infarctions.
2. Organic heart disease, etiology undetermined: (a) cardiac hypertrophy and dilatation; (b) RSR.
3. Acute pyelonephritis, recent.
4. Syphilis, tertiary, treated.

Dr. Jerome Kleinerman: At autopsy, the pertinent findings were in the heart and lungs. The main left pulmonary artery and the branches to the middle and lower lobes of the right pulmonary artery contained thrombi which were adherent to the vessel walls. There were two possible points of origin for these emboli: one, a mural thrombus in the right ventricle, and the other, phlebothrombosis of the left popliteal vein. Examination of the pulmonary emboli suggested that they came from the left popliteal vein and their age was relatively recent, unlike the more mature, organized thrombus in the right ventricle. The heart weighed 475 Gm. Figure 1 shows the right side of the heart. The tricuspid valve is normal in appearance, and in the lateral portion of the right ventricle, adjacent to the interventricular septum, and also involving its apical portion, there is an organizing mural thrombus. The myocardium underlying the mural thrombus is mottled brown and red and shows evidence of degeneration. Figure 2 is a close-up view of the mitral valve. The mitral valve shows definite evidence of old, healed rheumatic involvement. There is thickening and fusion of the chordae tendineae and hypertrophy of the papillary muscles. There is also thickening of the free edge of the mitral valve and some fusion of the valve leaflets. However, the mitral ring itself measured 10.5 cm. Of particular interest, is the small verrucous lesion which is present on the atrial surface of the anterior leaflet of the mitral valve. This has a granular and friable appearance, but microscopically it was com-
Fig. 3. Section of right ventricle with intramural branch of right coronary artery showing an organized, recanalized thrombus. In the upper portion of the field the organizing mural thrombus is present. The right ventricular wall shows destruction of muscle and replacement by fibrous tissue (Orcein stain for elastic tissue).

pletely fibrotic and organized, with no evidence of fibrin or bacteria. Our interpretation of this lesion is that it represents a healed endocarditis, probably bacterial. The coronary arteries on gross examination were pliable and free of disease, and histologic sections of the main branches of the coronary arteries bear this out. However, on section of the myocardium in the right ventricular area adjacent to the mural thrombus and degenerating myocardium, a rather large, intramural coronary artery was completely occluded by an organized, recanalized thrombus. Figure 3 is an elastic stain which shows the remnants of the elastic fibers in the wall. The myocardial tissue around this vessel shows fibrosis and some collagen formation. There is still some evidence of inflammatory cells; however, they are mostly lymphocytes and plasma cells, and there are few acute elements left. A few pigment-filled macrophages are also present. Little evidence remains of any necrotic muscle cells. The mural thrombus is organizing. This was interpreted as a healing myocardial infarct.

In trying to correlate the pathologic findings with the clinical picture, it is suggested that the sequence of events was as follows. This patient had a healed rheumatic mitral valvulitis and developed bacterial endocarditis. This bacterial endocarditis healed, or at least did not proliferate. One or part of a vegetation became dislodged and was carried to a branch of the right coronary artery, that is, coronary embolization occurred. This belief is supported by the facts, first, that the coronary arteries
other than the occluded vessel, adjacent to the infarcted area, are normal, and second, that there is a good source for embolization, namely, the lesion on the mitral valve.\textsuperscript{1} Hamann\textsuperscript{2} indicated that the process of embolization to small branches of the coronary arteries in subacute bacterial endocarditis occurs frequently and is often multiple. These multiple small emboli may cause no acute symptoms. It is difficult to implicate this process as a cause of myocardial failure, since patients with subacute bacterial endocarditis usually die of other complications before myocardial failure occurs. The evidence here strongly points to healing bacterial endocarditis of the mitral valve, but since this is conjectural, a positive anatomic diagnosis was not made.

Although the mitral valve is not the most frequent source of coronary embolus, at least three other cases are mentioned in the literature. Cases reported by Virchow,\textsuperscript{3} Welch\textsuperscript{4} and MacCallum\textsuperscript{5} are all cited by Saphir\textsuperscript{6} and accepted by him as verified cases of coronary embolization with vegetations of the mitral valve as the source.

The immediate cause of death was the multiple pulmonary embolization. The most likely source of the emboli was the phlebothrombosis of the popliteal vein.

\textit{Anatomic Diagnosis}

1. Recent pulmonary emboli, main left, and middle and lower branches of right pulmonary arteries.

2. Myocardial infarction, healing, of right ventricle and interventricular septum with organizing mural thrombus.

3. Organized, recanalized thrombus of branch of right coronary artery.

4. Healed rheumatic mitral valvulitis.

5. Cardiac hypertrophy and dilatation (475 Gm.).

6. Phlebothrombosis, left popliteal vein.

7. Chronic passive hyperemia of lungs and liver.

8. Healing focal acute pyelonephritis, left.

\textit{Note}: Since preparation of this case, Brunson\textsuperscript{7} has reported nine cases of bacterial endocarditis, in seven of which coronary emboli were demonstrated. In five cases, emboli were noted in the intramural branches of the coronary arteries in addition to those found grossly. In three of his cases, the mitral valve was the only possible source for embolization, and in three other cases, the mitral valve was involved in addition to other valves.

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