Recurrent Parietal Thromboendoocarditis

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A rare condition, which generally occurs in young adults and may simulate coronary disease, is discussed. The patients are afebrile, with low blood pressures, fast weak pulses and marked irregularities in cardiac rhythm. They are unresponsive to therapy and may survive initial attacks only to succumb to a recurrence. In the portions of the endocardium uninvolved by mural thrombi, there is marked collagenized subendocardial thickening devoid of elastic tissue. The etiology is unknown.

The purpose of this report is to describe two cases of a relatively rare and obscure endomyocardial affection, occurring in young adults, which appears to stem from varying degrees of endocardial thickening. This type of pathologic lesion gives rise to a fairly definite clinical picture, which, while non-specific, is nevertheless to be considered in cases of atypical subacute to chronic myocardial failure in the absence of demonstrable coronary or valvular disease, either clinically or at autopsy. The lesion consists of collagenous thickening of the subendocardial connective tissue with superimposed ulceration of the overlying endocardium. This is followed by a florid proliferation of the subendocardial connective tissue into the trabecular carnea and along the vascular septa of the myocardium, with eventual mural thrombus formation and its sequelae of peripheral embolization.

Case Reports

Case 1.

A 34 year old white man was admitted to Murphy General Hospital on July 28, 1948, with shortness of breath on exertion, weakness, nocturnal dyspnea, weight loss, and pain in the paraumbilical region of the abdomen occurring two to three hours after meals.

At the age of 12, cervical lymph nodes on the left side had been removed for “swelling.” The diagnosis on the removed nodes is not known. No further lymphadenopathy was noted. In 1946 he first complained of recurrent abdominal pain following meals and the diagnosis of duodenal ulcer was made. He received treatment for this condition and was again admitted to the hospital in 1947. Electrocardiograms taken at that time were abnormal, but no definitive diagnosis of heart disease was made. On further questioning, the patient stated that he had been told in 1942 that he had “heart disease” but did not know what diagnosis had been made.

There was no past history of rheumatic fever or syphilis.

From 1946, the symptoms of chronic cardiac failure became progressively worse.

Physical examination, on admission, revealed a pulse rate of 132, blood pressure 90/70, and no dyspnea at rest. The heart was enlarged to the left, and to a lesser extent to the right. The pulse was weak, threadlike, and gallop rhythm was heard at the apex. No murmurs or friction rubs were observed. The lungs were clear, and there was no fluid in the abdomen. The liver edge was palpable below the right costal margin. The remainder of the physical examination was noncontributory. Fluoroscopy of the heart on July 29, 1948, was considered fairly characteristic of pericardial effusion. His admission electrocardiogram showed marked left axis deviation and inversion of all T waves. This was almost identical to the electrocardiographic findings six months earlier. The initial impression was pericardial effusion, probably of a tuberculous nature. Later electrocardiograms taken Sept. 20, 1948 disclosed findings consistent with pericarditis (fig. 1).

The laboratory findings on admission showed a hemoglobin of 80 per cent, a white blood cell count of 10,700 with a normal differential, hematocrit of 43, and a sedimentation rate of 24 mm. in one hour. Urinalysis showed a specific gravity of 1.026 and a trace of albumin. It was otherwise normal. Serology was negative. Repeated sputum examinations for tubercle bacilli were negative. The total protein was 5.3 mg. per cent. Chest roentgenologic examination in August, 1948, revealed an enlarged heart with evidence of right lower lobe pneumonia. On Feb. 4, 1949, there were scattered areas of pneumatic infiltration in both lower lobes with the possibility of superimposed pulmonary infarction.

The clinical findings, together with a history of cervical adenopathy in childhood, a positive tuberculin test, and slight apical infiltrations by x-ray examination, led to the institution of streptomycin therapy on the basis of a probable tuberculous pericarditis. This therapy, however, did not alter the course of the disease, and despite digitalis and supportive measures, the patient failed to improve. There were recurrent acute attacks of dyspnea and
tachycardia. His pulse rate varied from 80 to 160 during the hospital course, with average rates of 100 to 120. On Jan. 25, 1949, clinical thrombo-phlebitis involving the right leg was discovered. The prothrombin time was markedly prolonged, being only 16.4 per cent of normal, and anticoagulant therapy was begun cautiously and then stopped because of apparent liver damage. Repeated prothrombin times were essentially the same, and the patient evidenced clinical jaundice for the first time on Jan. 30, 1949. The liver was tender and extended four finger breadths below the right costal margin. On Feb. 8, 1949, he developed severe dyspnea, stupor, and finally expired.

**Gross Necropsy Findings.** The heart weighed 330 Gm. A gray, fibrous membrane covered the epicardial surfaces of both ventricles, and the pericardial cavity contained about 80 cc. of clear, bile-stained fluid. The chambers were dilated. The myocardium was flabby and pale tan-yellow in color. The parietal endocardium of the left ventricle was covered with a layer of adherent, gray, opaque fibrous tissue with massive mural thrombus formation at the apex. The coronary arteries were normal in origin and distribution, and were widely patent throughout. The valves were normal. There were no verrucae or vegetations. The left ventricular wall measured between 12 and 16 mm. in thickness, and the right 2 to 4 mm. The right lung weighed 900 Gm. A large, firm, reddish brown, wedge-shaped area was noted in the right upper lobe. Two similar but smaller areas were present in the right lower lobe. Adherent thrombi, occluding the lumina, were found in branches of the pulmonary artery leading to these areas. The left lung weighed 550 Gm. and, on section, large quantities of edema fluid oozed from the cut surfaces. The liver weighed 1270 Gm. and on section had a “nutmeg” appearance. The spleen weighed 150 Gm. and was moderately congested. The right kidney weighed 160 Gm., the left 145 Gm. Neither kidney was grossly remarkable. The gastrointestinal tract was normal, with the exception of an old healed duodenal ulcer. The remaining organs, with the exception of the brain, which was not examined, were normal.

![Fig. 1. There is left axis deviation with sinus tachycardia. T waves are inverted in leads I, II, and CF$_1$; diphasic in CF$_2$ and CF$_3$.](image1)

**Fig. 2. Case 1.** There is a superficial layer of fibrin. Beneath it the subendocardial collagen is thickened. (Mallory aniline blue stain, ×35.)

**Microscopic Findings.** The lining serosal cells of the epicardium showed considerable hypertrophy, assuming a somewhat polygonal to cuboidal form with fairly large, vesicular, round to spherical nuclei. Sparse lymphocytic infiltrations were noted. One section, through all coats of the right ventricle, disclosed a rich hyperplasia of collagenous connective tissue involving the epicardial fat in one area, and strongly resembling that seen in the endocardium. There was slight myocardial edema, and focal zones of sclerosis were evident in the subendocardial areas. Little or no sclerosis was seen in the deeper myocardium. The subendocardial collagenous connective tissue was markedly thickened. (See fig. 2.) In some areas it was fairly cellular; in others, it assumed the appearance of a somewhat amorphous ground substance. Special stains revealed that this increased thickness was due to the deposition of large quantities of collagen in the subendocardial region. There was practically no elastic tissue at this site. The collagen in this location was similar to that composing the underlying bands which extended into the myocardium along the perivascular connective tissue septa. There was a large organizing
thrombus composed of large masses of red cells, fibrin, proliferating small blood vessels, and numerous lymphocytes overlying the thickened endocardium (fig. 3). Islands of persisting viable myocardium were pinched off and surrounded by collagenous connective tissue. Similar thrombi filled the buys and extended into the thebesian veins.

Chronic passive congestion, atelectasis, and hemorrhagic infarction were demonstrable in the lungs. The liver showed severe chronic passive congestion with hemorrhagic central necrosis. There was moderate chronic passive congestion of the pancreas, spleen, and kidneys. The adrenals showed slight lipid depletion and congestion. Chronic inflammation of the stomach and duodenum was present. A section of omental fat revealed a sclerotic thickening of the serosa.

**Case 2.**

A 27 year old white man was admitted May 2, 1950 to the hospital at Fort George G. Meade, Md., with abdominal pain of approximately one month's duration, followed by ankle swelling and dyspnea of 10 days' duration. There was no past history of rheumatic or venereal disease. He was well until approximately one month prior to admission at which time there was an abrupt onset of persistent postprandial nausea and vomiting of undigested food, followed later by generalized aching abdominal pains. Ten days prior to admission he noted mild dyspnea without orthopnea, followed by swelling of the lower legs and ankles. Physical examination on admission disclosed a temperature of 97 F, an imperceptible pulse with an apical rate of 136, respirations of 20, and an unobtainable blood pressure. He was acutely ill, with slight cyanosis of the lips, reddish-purple blotches on the skin, a generalized, excoriated, maculopapular rash, and a few small ecchymoses. Chest examination revealed a few moist rales at the bases, and the heart was slightly enlarged to the left. The sounds were fairly sharp with a gallop rhythm heard best at the apex. No murmurs were noted. There was generalized abdominal tenderness and slight distention. The liver was palpable two finger breadths below the right costal margin. The penis was edematous, and there was 4 plus pitting edema as high as the knees and to a lesser extent over the thighs and abdomen.

He was placed on oxygen, digitoxin, and Mercuhydrin therapy, but failed to respond. The tachycardia, gallop rhythm, edema, and rales persisted. Blood pressures varied between 75/60 and 90/80. On May 9, 1950, he first showed persistent clinical jaundice. On May 20, 1950, he vomited 500 cc. of fresh and clotted blood, and died shortly thereafter.

**Gross Necropsy Findings.** On external examination, the body was that of a well developed, rather obese, 27 year old white male, weighing approximately 225 pounds and measuring 68 inches in length. There were 250 cc. of clear amber fluid in the peritoneal cavity. The stomach was markedly distended and the appendix absent.

The heart weighed 430 Gm. and the pericardial cavity contained 90 cc. of clear amber fluid. The myocardium proper presented no gross lesions. In the apical area of the left ventricle, a friable, pinkish-white opaque mass, measuring 1.5 cm. in diameter, was attached to the endocardium. A similar mass of friable tissue presented on the right auricular endocardium, and measured 1.0 by 1.0 by 1.5 cm. The left auricular endocardium was smooth and the right ventricle somewhat dilated. The valves were normal. The coronary arteries showed minimal intimal atherosclerosis, with no evidence of luminal obstruction. The endocardium was somewhat opaque and appeared thickened in areas. The aorta was smooth and elastic. The right lung weighed 570 Gm., left, 430 Gm.; both were edematous and congested on section. The tracheobronchial tree was clear. The liver weighed 1660 Gm. and on section had a "nunmeg appearance." The gall bladder and extra hepatic biliary tract were normal. The pancreas and spleen were grossly normal. The right kidney weighed 220 Gm., the left, 200 Gm. Neither kidney showed any gross lesions. The remainder of the genitourinary tract was normal. The adrenals and thyroid were normal. A small area of intense engorgement was noted in the prepyloric region of the stomach. The remainder of the gastrointestinal tract was normal. The brain was not examined.

**Microscopic Findings.** A section through the apex of the left ventricle disclosed a large mural thrombus overlying a markedly thickened endocardium. There was beginning organization at the base, with capillary proliferation. There was fresh hemorrhage in the subendocardial areas. Sections through the

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**Fig. 3.** Case 1. Discloses mural thrombus with underlying thickened endocardium. (Hematoxylin and eosin stain, ×35.)
septum membranaceum, and through the left auricular endocardium, disclosed entrapment of the myocardial conduction tissue in the thickened endocardium. The lungs showed congestion, edema, and focal hemorrhages. Recent severe hemorrhagic central necrosis was manifest in the liver. The pancreas, spleen, kidneys, and remaining organs were not remarkable.

**Discussion**

In reviewing the literature on diseases of the mural or parietal endocardium, descriptions of hearts showing varying degrees of endocardial thickening under a variety of names and differing circumstances are frequently encountered. This change is sometimes the result of a diffuse fibroelastosis, such as is found in certain congenitally malformed hearts; at other times, the picture is simply one of moderate sclerosing edema and collagenization of the subendocardial space, as may be seen in some cases of widespread scleroderma; still another pattern may show endocardial fibrosis as one of reparative fibrosis associated with inflammation, infarction, or thrombosis. For example, endocardial thickening may follow primary coronary disease. Certain cases of subacute bacterial endocarditis may spread from the valves to involve the adjacent auricular and ventricular endocardium. Inefficient valves, with extensive regurgitation, may lead to endocardial scarring. Rheumatic and diphtheritic myocarditis may involve the mural endocardium and heal with scar formation. Weiss and others\(^1\) described endocardial thickening in association with scleroderma. Schürmann and MacMahon\(^ 2\) described similar changes in patients with malignant nephrosclerosis, thrombophlebitis, and periarteritis nodosa. Recently, we have had the opportunity to study the same lesion in a classic case of disseminated lupus erythematosus. Dock\(^3\) has included endocardial thickening as a histologic component of the beriberi heart. In most, if not all, of these cases, this endocardial change has played little or no recognizable part in the clinical symptomatology of the systemic disease under discussion and the lesion has been but an incidental autopsy finding.

In the two cases under consideration, the changes involving the endocardium dominated both the clinical picture and the autopsy findings. In brief, we recognize the possibility that this lesion may appear as a component of more complex clinical and anatomic syndromes, but we would like to emphasize that this condition alone may simulate coronary disease and that it may, as an isolated disease entity, lead to death.

Davies\(^4\) described a great number of cases of endocardial fibrosis occurring in African natives, and his clinical and anatomic descriptions coincide strikingly with the lesions found in our two cases. His cases showed either endocardial necrosis with secondary thrombosis, or diffuse subendocardial sclerosis. Bedford and Konstam\(^ 5\) reported 40 cases of unexplained heart failure in West African troops serving in the Middle East in whom subendocardial fibrosis was a prominent anatomic feature. Smith and Furth,\(^6\) in 1943, published a report of three cases of fibrosis of the endocardium complicated by mural thrombosis; Gray\(^7\) reported two similar cases in Europeans living in West Africa, and in a recent abstract, Dammin, Glaser and Roberts\(^8\) called attention to this same type of lesion.

**Clinical Features.** Most patients suffering from this disease are young adults. In our cases the ages were 34 years (case 1), and 27 years (case 2). Other case reports list the ages of patients with this syndrome as: 15 years,\(^9\) 23 years (2 cases),\(^10\) and between 20 and 30 years.\(^2\) In Davies\(^4\) series, death occurred most commonly in adolescence and early adulthood. Sex appears to be of little importance. These patients present clinically a rapid, weak pulse. In our second case the pulse rate was unobtainable at a stage during which the apical rate was 136. The blood pressure is low-normal, or occasionally unobtainable. Hypertension was not encountered in our cases, and other reports seem to agree with this observation. Rather marked disturbances of cardiac rhythm, including gallop, are common. The electrocardiogram is abnormal but not diagnostic. The course, if uncomplicated, is afebrile.

In case 1 slight temperature rises were noted, which were explainable on the basis of a transient bronchopneumonia, pulmonary infarction, and thrombophlebitis. Clinically, the hearts, both by physical and x-ray examination, show enlargement usually to the left, but
right-sided enlargement may also be seen. The findings on physical examination are those usually encountered in cases of myocardial failure and are related to the duration of the illness as well as to the extent of the pathology found at autopsy. Any bizarre manifestations of the diseased endocardium may be observed, including embolic accidents involving any of the viscera or extremities. Again, secondary thrombophlebitis following bed rest, with subsequent pulmonary embolism, may occur (case 1). The course of the disease is quite variable. Some patients may die in the first severe attack; others, unresponsive to all therapy, may survive less severe attacks only to succumb to repeated bouts of myocardial failure.

Present laboratory findings seem to be of little aid in the diagnosis. Davies8 has found a transient eosinophilia in some of his cases, the cause of which is unknown. Both of Gray’s7 cases showed a high, but difficult to explain, eosinophilia. He stated, however, that both of his cases had Loa loa infestations, which could easily account for the eosinophilia. The probability of parasitic infestations in Davies’ cases cannot be overlooked. No eosinophilia was noted in either of our cases.

Pathologic Features. Microscopic examination of the endocardium in areas free of mural thrombi disclosed a very homogeneous, uniform type of subendocardial thickening consisting almost entirely of collagen. In some areas the collagen had the appearance of an eosinophilic ground substance, distinctly different from scar tissue. In other locations the collagen was fairly cellular and contained numerous spindly fibroblasts. This collagen had filled the subendocardial areas and caused a tremendous thickening of this layer. It had enveloped the myoneural tissue of the cardiac conduction system and spread along the vascular septa of the myocardium. In areas with overlying mural thrombus formation, the thrombi were perpetuated into the bays and along the endocardium of the trabeculae, producing a sequential thrombosis of the thebesian vein system at that site. Similar observations have been reported by Flynn and Mann.11

In areas of mural thrombus formation, it is practically impossible to differentiate endocardium, subendocardial connective tissue, and subendocardial myocardium. Nevertheless, in areas free of thrombi or adjacent to thrombi, this distinction is rather apparent and the involvement here is primarily in the subendocardial connective tissue. That the entire process is initiated from within out, that is, from endocardium to myocardium, is further attested to by the fact that the deeper myocardium is essentially free of primary disease. Bacterial stains failed to reveal the presence of any organisms in all of the areas examined. The inflammatory response appears to be entirely nonspecific, and in the healing process, there is a virtual absence of elastic tissue formation. This latter finding alone would seem to separate this entity from the fetal type of endocardial fibroelastosis described by Gross12 and more recently, by Prior and Wyatt,13 in which the elastic component is very conspicuous.

The sequence of events would appear to be as follows: First, there is an accumulation of a relatively cell-free fluid ground substance immediately beneath a swollen layer of endothelial cells which form the inner endocardium. This undergoes sclerosis and collagenization and may extend in between the adjacent muscle fibers. This basophilic material, now appearing as ground substance, may accumulate to such an extent that it may bulge above the level of the adjacent endocardium. It may constrict and even close the large venous sinuses reaching into the inner third of the myocardium. This change may be complicated by hemorrhage and recurrent thrombosis. One or all of these changes may recur so that older lesions, complicated by repair, organization, and pigmentation, may become increasingly complex and difficult to interpret. The underlying muscle, during the active phase of this process, can show atrophy, hydropic degeneration and necrosis.

The functional significance of this lesion depends on the type of reaction, its location, extent, and complications. In the two cases under discussion, the subendocardial tissues of the left ventricle were primarily involved. There was massive interventricular thrombosis, occlusion of venous sinuses, degeneration and necrosis of muscle fibers, and sclerosis of muscle bundles, all in the area in which the con-
duction system is most heavily concentrated. These findings could reasonably be correlated with the clinical symptoms and the electrocardiographic tracings.

The etiology of this disease is unknown. Even the nature of the lesion and its pathogenesis remain obscure. At best it seems to fall into the inflammatory group of diseases, dominated in its early stages by an exudation or accumulation of cell-free, protein-rich fluid into the subendothelial tissue spaces. In its later stages, sclerosis and collagenization of this intercellular ground substance is present. If there is hemorrhage or thrombosis, the pattern is complicated by organization and repair. The regressive changes, involving the underlying parenchymatous tissue which may play such an important functional role, would appear to be secondary and dependent upon the primary lesion in the interstitial spaces. There have been many hypotheses to explain the lesion, but none has been fully satisfying. One step, and possibly the first, would seem to be a change in the overlying endothelium, altering its permeability, and lowering the threshold of exchange between circulating blood and tissue fluids. Schürmann and MacMahon postulated such an hypothesis to explain the vascular and parenchymatous lesions common to malignant nephrosclerosis, periarteritis nodosa, and scleroderma.

**Summary**

Two cases of a relatively obscure endomyocardial affection of unknown etiology have been presented. Each had a similar unresponsive clinical course manifested by chronic myocardial failure, and atypical clinical signs with negative cardiac histories. Each case had one common postmortem finding, characterized by a sclerosis and thrombosis of the parietal endocardium of the left ventricle. The coronary arteries and valve leaflets in each case were essentially healthy. It is recognized that endocardial sclerosis and even endocardial thrombosis may occur as a relatively incidental finding in some of the so-called collagenous diseases, but it is the purpose of this paper to point out the fact that this same lesion may occur to a remarkable degree in an isolated form and that it may lead to death. The fact that this condition appears in young adults, mainly below the age of 40, should serve as a stimulus to its further elucidation.

**SUMARIO ESPAÑOL**

Se discute una condición rara que generalmente ocurre en adultos jóvenes y puede simular enfermedad de las coronarias. Los pacientes son afibrile, la presión arterial es baja, el pulso es débil ligero y con marcadas irregularidades en ritmo cardíaco. La condición no responde a tratamiento y los pacientes pueden sobrevivir ataques iniciales solo para sucumbir en una recala. En las porciones del endocardio no envueltas por trombos murales hay espesamiento subendocardiaco colagenizado despropósito de tejido elástico. La etiología es desconocida.

**REFERENCES**

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