Focal Necrotizing Myocarditis without Interstitial Infiltration

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Sudden death occurred in a patient considered to have a myocardial infarction. Detailed microscopic examination revealed a focal necrotizing myocarditis without interstitial infiltration. The original connective tissue framework without collagen in many of the areas where muscle fibers disappeared precludes the term myocardial fibrosis. A pathologic classification is suggested. No adequate etiologic agent could be found.

There are many reports in which myocardial disease of unknown etiology has been the sole pathologic abnormality.1-3 Most authors have grouped these cases of isolated myocarditis together, although many of the reports lack sufficient clinical and histologic detail for adequate comparison. As a result, objections to this grouping have been recorded.3-5 It seems important, therefore, to report these rare cases in sufficient detail so that in the future they may be grouped properly. The following case report of myocarditis of unknown cause is accordingly given in detail.

Case Report

L. H. (CVAH 21253) a white male, tool die maker, aged 46, was admitted to the hospital because of substernal pain of two days' duration. He had had measles, mumps, chicken pox, and whooping cough in childhood. Twenty years previously a diagnosis of duodenal ulcer had been made. He had consumed large amounts of alcohol throughout many years. Otherwise his past and family histories were non-contributory.

For seven years he had had infrequent episodes of substernal burning occurring at rest and on exertion, which lasted up to 10 minutes and were relieved by baking soda. During the preceding four months these attacks increased in frequency and severity and were no longer relieved by soda. Two days before admission, after supper, he experienced a burning pain in the epigastrium which increased in intensity despite soda and an unsuccessful attempt to vomit.

The pain gradually spread substernally, to the left axilla and down the inner aspect of the left arm. It was promptly relieved by an injection of morphine. During the next two days, there was recurrence of this pain on several occasions, relieved only by further morphine injections.

Physical examination on admission showed a well developed and well nourished, but slightly cyanotic white man. The temperature was 98.6°F., pulse 96, respirations 22, and blood pressure 138/106. There was no distension of the neck veins. The lungs were clear. The heart was not enlarged. There were no murmurs. The remainder of the physical examination was entirely negative.

The blood Kahn reaction was negative, the hemoglobin 15.8 Gm. per 100 cc., the hematocrit 54 per cent. The white cell count was 5350 with a normal differential. The cholesterol was 231 mg. per 100 cc. Repeated urine examinations were negative. X-ray films of the chest were normal. The initial electrocardiogram showed diphasic T waves in chest leads V3, V4 and V5 without any displacement of S-T segments or abnormalities of the QRS complexes.

The diagnosis of myocardial infarction was entertained. Treatment consisted of complete bed rest, oxygen, morphine, and dicumarol. However he continued to have intermittent episodes of substernal pain. On the seventh and eighth hospital days he suffered moderately severe attacks of substernal pain, and on the twelfth day a markedly severe attack in which he became cyanotic, pulseless and suddenly expired. During his week in the hospital electrocardiograms made at frequent intervals showed deep inversion of T waves in all the chest leads which began to recede toward normal and subsequently again become inverted.

 Necropsy. The body was that of a well developed and well nourished man with abundant deposits of fat. There was no edema. The peritoneal cavity was normal. Both pleural cavities were obliterated by firm, fibrous adhesions. The left lung weighed 725, the right 825 Gm., and on section both presented a grey spongy surface in the soft crepitant portions from which a small amount of grey fluid was expressed. A reddish-purple meaty surface presented in

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the firm, less crepitant portions from which a large amount of red, frothy, thin fluid was expressed. Abundant, turbid, mucoid fluid was present in the bronchi and bronchioles.

The heart weighed 450 Gm. The chambers were not dilated. The epicardium was smooth. Irregular, light-brown foci were found throughout the myocardium of the left ventricle. In the posteroinferior portion of the interventricular septum, soft, irregular, poorly-demarcated, reddish-brown foci measuring 0.3 by 0.3 cm. were seen. Yellowish-white streaks extended from this region. The myocardium of the right ventricle was homogenous, reddish-brown. The endocardium and valves were negative. The coronary arteries displayed infrequent, small yellowish plaques, but the lumina were not narrowed. No thrombi were found. The tricuspid valve measured 12.5 cm., the pulmonic valve 8.0 cm., the mitral valve 10.5 cm., and the aortic valve 6.5 cm. The left ventricular wall measured 2.0 cm., and the right 0.5 cm. in thickness. A few small yellowish plaques were found in the lumbar portion of the aorta. The spleen weighed 250 Gm. The pulp was deep purple, moist, with no fibrosis. The liver weighed 2150 Gm. The capsule was smooth, and thin. The sectioned surface was reddish-brown, moist, with light brown zones about moderately prominent central veins.

**Microscopic Examination.** The tissues were fixed in Zenker's fluid. Hematoxylin-eosin, Mallory's aniline blue collagen, Verhoeff's elastic tissue and Perdrau's reticulum stains were used. The visceral pericardium was negative. In the myocardium of the left ventricle infrequent small groups of acidophilic granular muscle fibers with absent striations were infiltrated by a few neutrophils. Prominent in sections of the interventricular septum and of the wall of the left ventricle were large and small foci of necrosis containing the original myocardial supporting framework from which the muscle fibers had disappeared. In some areas, small groups of normal muscle fibers could be found surrounded by these foci. The original pattern of the myocardial supporting framework within these foci was often well preserved and could easily be recognized by the open meshwork of elongated linear collagenous strands running in a parallel order, surrounding spaces from which the muscle fibers had disappeared (figs. 1 and 2). These linear collagenous strands were usually closer together than in regions where the myocardium was intact. The reticulum stain revealed coarse, elongated silver-positive strands closely applied to the collagen strands observed in the aniline blue collagen stain (fig. 3). There were a few foci of necrosis where the deposition of slightly abundant collagen had taken place (fig. 4). Here the original supporting framework was not as obvious with the aniline blue collagen stain, but it could still be seen with the reticulum stain although much compressed. Small, dilated, thin-walled blood vessels were visible within these foci of necrosis, but no elastic tissue was found. A few scattered pigmented and non-pigmented histiocytes, lymphocytes, eosinophils, and neutrophils were observed in the foci of necrosis. No cellular infiltration of the unaltered interstitial tissue was found. Infrequent swollen nuclei were present within the muscle cells at the borders of the foci of necrosis. Moderate fatty tissue infiltration was noted in the myocardium of the right ventricle. A few arterioles and pre-arterioles within the myocardium of both ventricles displayed slightly thickened walls. Small arteries infrequently possessed slightly thickened fibrotic intimal layers, but no narrowing of the lumina was found. The coronary arteries infrequently displayed slight fibrous thickening of the intimal layer. The intima of the aorta was slightly thickened by fibrosis with rare vacuolated histiocytes observed. There was moderate congestion of the liver and the spleen. Other organs were normal.

**Discussion**

The most common causes of necrosis of muscle fibers leading to fibrosis of the myocardium are vascular insufficiency and infections. In this case there was no evidence of either. Rivers has indicated that when viruses act with explosive rapidity or when the in-
Fig. 2. Left ventricle. Early lesion. Places from which the muscle fibers have disappeared in a focus of necrosis are surrounded by collagenous strands of the unaltered supporting framework. Verhoeff's elastic tissue stain. Magnification × 475.

Fig. 3. Left ventricle. Reticulum fibers of original supporting framework are more closely approximated than normal but the general pattern is still maintained within a focus of necrosis. Perdrau's reticulum stain. Reduced from original magnification × 475.

Fig. 4. Left ventricle. Older focus of necrosis with slight deposition of collagen and condensation of the original supporting framework. Mallory's aniline blue collagen stain. Reduced from original magnification × 100.

Volved cells are incapable of division the primary pathologic changes are necrobiosis and lysis of cells. Covey has suggested that this explosive lytic change takes place in isolated myocarditis. The possibility that a virus was
the etiologic agent in the case reported above cannot be ruled out. There was no evidence for metabolic or dietary disturbances which have been suspected as a cause in some cases.10,11

Lytic changes and disappearance of cells with preservation of the original supporting connective tissue framework with no collagen deposition in many of the foci of necrosis suggest a subacute process. This is consistent with observations made by Mallory, White and Salcedo in myocardial infarction.12 Previous reports of cases interpreted as myocardial fibrosis similar to the case reported here do not exclude the possibility that the connective tissue foci actually represented the original connective tissue framework without collagenization.13-15 Some of these cases may also represent comparatively early lesions. The term fibrosis should not be applied to foci of necrosis in which an intact supporting framework is still present and no collagenization has taken place.

The lack of interstitial infiltration in this case was noteworthy. Interstitial infiltration has been found in many cases of isolated myocarditis to which the term "Fiedler's" has been applied. Extensive interstitial infiltration in the complete absence of muscle necrosis has also been reported.16 The cellular infiltrate observed here within the foci of necrosis was similar to that found in any phagocytic process following the removal of necrotic cardiac muscle fibers and did not appear to be due to a specific etiologic agent. It would appear then that it is possible to have either interstitial myocarditis or focal necrotizing myocarditis with or without interstitial infiltration. It is not possible at present to state whether a single cause is responsible for all of these pathologic changes.

The changes described in the case reported and in cases previously reported do not offer a distinctive clinical picture which could be recognized ante mortem.

SUMMARY

A case of focal necrotizing myocarditis without interstitial infiltration is reported. The preservation of the original connective tissue framework and the lack of collagenization in many of the regions where muscle fibers had disappeared indicated a subacute process and precluded the use of the term "myocardial fibrosis." No adequate cause could be found. The patient presented the clinical picture of myocardial infarction. A histologic classification of these cases is suggested.

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