ENDOMYOCARDIAL FIBROSIS IN THE CEYLONISE

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Received April 30, 1958

Several papers dealing with endomyocardial fibrosis have appeared in recent years, most from Africa (Bedford and Konstam, 1946; Edge, 1946; Gray, 1951; Davies and Ball, 1955), a few from America (Smith and Furth, 1943; Elster et al., 1955), and from Europe (Löfler, 1936; Mümme, 1940). It differs from fibrosis of the endocardium and myocardium accompanying occlusive disease of the coronary arteries, anomalous origin of the coronary arteries, congenital fibro-elastosis and the fibrotic forms of nutritional cardiopathy. In endomyocardial fibrosis there is no disease of the coronary vessels and fibrosis is mainly confined to the endocardium and the myocardium underlying it.

Information regarding geographical and racial distribution is scanty. It was thought worthwhile, therefore, to report three cases of endomyocardial fibrosis in the Ceylonese.

CASE REPORTS

Case 1. A man, aged 23, was admitted with a history of fever, difficulty in breathing and swelling of his lower limbs. He had no history of rheumatic fever. On examination he was jaundiced. His heart was enlarged, the apex beat being in the 6th intercostal space in the anterior axillary line. There was a systolic and a doubtful presystolic murmur in the mitral area.

The lungs were normal. The liver was palpable three fingerbreadths below the right costal margin. The spleen was not palpable. On fluoroscopy there was marked enlargement of the left auricle and right ventricle and the pulmonary conus was prominent. The jaundice improved and he was discharged in three weeks with a diagnosis of mitral stenosis with right heart failure and infective hepatitis. He was readmitted two months later. His condition gradually deteriorated and he died five days after admission.

Post-Mortem Findings. Heart. There was a haemorrhagic pericardial effusion. The auricles were dilated. The right ventricle showed slight fibrosis of the endocardium at its apex. The left ventricle was normal in size and its endocardium was completely fibrosed. There was an ante-mortem thrombus at the apex of the left ventricle. The valves, coronary arteries and their orifices were normal. The right internal jugular vein was cord-like but no ante-mortem thrombus was detected. Lungs. There was blood-stained effusion on the right, and a small infarct in the base of the left lung. The liver was enlarged and "nutmeg".

Histological Appearances. The cardiac muscle showed fibrosis of the endocardium and the underlying myocardium, with a mural thrombus on the endocardium. The lungs showed infarction and in some areas oedema and haemorrhage into the alveoli. The liver and spleen showed congestion.

Case 2. A woman, aged 37, was admitted with a history of breathlessness on exertion, and swelling of the lower limbs of two months duration. Her past history revealed that she had had three attacks of swelling of joints associated with fever, since the age of 25 years. On examination her nutrition was poor. She had a raised jugular venous pressure. The heart was enlarged with doubtful presystolic and systolic murmurs in the mitral area. Râles were heard over both lungs. The liver was enlarged and she had ascites. On fluoroscopy the left auricle was enlarged. She was discharged after three weeks with a diagnosis of
mitral stenosis and congestive heart failure. She was re-admitted two months later and died within two months.

Post-Mortem Findings. Heart. The pericardial sac contained an ounce of serous fluid. The right auricle had a large ante-mortem thrombus in the auricular appendix and a small one near the opening of the coronary sinus. The right ventricular muscle was hypertrophied, the chamber dilated and the wall fibrous. The left auricle was normal. The left ventricular muscle was firmer than usual. The valves were normal. There were bilateral pleural effusions. The left lung was oedematous, with evidence of bronchopneumonia. There were ascites and the liver was enlarged.

Histological Appearances. The heart muscle showed atrophy and hyaline changes with an increase in fibrous and connective tissue in the endocardium and in the myocardium underlying it. In the fibrous bands there were thin-walled dilated vessels. The coronary arteries and valves showed no abnormality. The lungs were oedematous and congested. The liver was congested. The spleen and kidneys were normal.

Case 3. A man, aged 25, was referred as a case of constrictive pericarditis suitable for surgical treatment. He gave a history of dyspnoea of one month's duration, oliguria, and oedema of the lower limbs. He gave no history of rheumatic fever. On examination he was orthopnoeic, his jugular venous pressure was raised, and his pulse paradoxical. The blood pressure was 175/140 mm. Hg. The heart was grossly enlarged and the apex beat was felt in the 6th intercostal space in the mid-axillary line. There was a systolic murmur and a protodiastolic gallop at the apex. Crepitations were heard in the lungs. The liver was enlarged and tender. There was free fluid in the abdomen. The electrocardiogram showed left ventricular hypertrophy. Fluoroscopy revealed an enlarged heart with marked pulsation of all its chambers. It was clear that this patient had some odd type of cardiac enlargement and, in the last stages of his illness, pericarditis nodosa was considered, but there seemed to be nothing to support this diagnosis other than his hypertension. He came to autopsy seven weeks later with a diagnosis of secondary hypertension of obscure aetiology, possibly pericarditis nodosa, possibly obscure nephritis.

Post-Mortem Findings. Heart. The pericardium was normal. The pericardial sac contained 3 ounces of straw-coloured fluid. The heart was about twice its normal size. The great veins were dilated. The pulmonary artery was twice its normal size. The right auricle and ventricle were dilated. The left auricle was apparently normal. The left ventricle was enormously dilated and hypertrophied. There was a large white patch at the apex of the left ventricle about 4 x 3 cm. and 3-4 mm. in thickness involving the endocardium. It was firm, fibrotic, and fairly well defined. The fibrotic layer was seen to extend as a thin strand in the myocardium along its cut end, 2-3 mm. away from the endocardial surface. There was a large thrombus at the apex over the fibrotic patch.

The valves were normal. The aorta and the coronary arteries showed no abnormality. The lungs were congested. There was ascites and the liver had a "nutmeg" appearance. The spleen was enlarged and congested. The kidneys were a little less than normal in size. The capsule stripped easily and the surface was granular and slightly reddish. The cut surface showed no abnormality. The appearance was that of a "red granular kidney".

Histological Appearances. The endocardium was thickened by loose fibrous tissue. Overlying the thickened endocardium was a fibrin thrombus. The left ventricle and to a lesser extent the right showed these changes. Bands of fibrous tissue were seen extending into the myocardium (Fig. 1). In the fibrous bands were numerous thin-walled dilated vascular channels (Fig. 2). The myocardial fibres showed atrophy, hyaline changes and interstitial oedema. The coronary arteries showed no abnormalities in the larger vessels but obliterator changes were seen in some of the smaller vessels in places where the endocardial fibrosis was pronounced. The valves and the atria were normal. The lungs showed infarction with oedema and haemorrhage into the alveoli. The liver and spleen showed congestion. Kidneys. The appearances were compatible with pyelonephritis which was probably responsible for the hypertension.

DISCUSSION

There are a multiplicity of possible factors in the formation of endomyocardial fibrosis and they are the subject of very divergent views. Endomyocardial fibrosis has been confused with beri-beri heart disease, nutritional heart disease, cardiac collagenosis, congenital fibro-elastosis, and isolated myocarditis. Malnutrition has been suggested as a cause of endomyocardial fibrosis. Prolonged vitamin B1 (thiamine) deficiency predisposes to beri-beri heart disease and is characterized by hyperkinetic circulation, vasodilation, enlargement of the heart, and peripheral oedema. Wood
Fig. 1.—(A) Thickening of the endocardium and subendocardium; (B) thin-walled vessels; (C) penetration of the myocardium with fibrous tissue in trabecular fashion. Hematoxylin and eosin. Magnification, x 30.

Fig. 2.—Several thin-walled vessels in the fibrous layer of the subendocardium. Haematoxylin and eosin. Magnification, x 110.
(1956) states that in this condition the heart shows little pathological change at necropsy, the disturbance being biochemical rather than structural. In endomyocardial fibrosis, injections of vitamin $B_1$ produce no response (Ball, 1957). Gillanders (1951) described a nutritional cardiopathy quite unlike that of beri-beri, in that it was unaffected by vitamin $B_1$ and was further associated with liver disease: he found no evidence of subendocardial fibrosis and necrosis in any of his cases. Liver diseases of the kind often associated with malnutrition are fatty infiltration, cytosiderosis, and cirrhosis (Gillman and Gillman, 1945). Bragdon and Levine (1949) report the occurrence of myocardial lesions in rabbits in vitamin E deficiency. Davies’ (1948) cases were all malnourished with fibrosis involving the endocardium and myocardium and mural thrombi: they are very similar to cases in the present report. Bedford and Konstam (1946) described 17 necropsies in African troops who were having a well-balanced diet and found fibrosis mainly to be subendocardial.

Becker et al. (1953) claimed that endomyocardial fibrosis was a collagen disease. Gray (1951) drew attention to the resemblance of the lesions to sclerosis and certain cases of disseminated lupus erythematosus. Cases of sclerosis that had developed heart failure showed fibrotic changes throughout the whole myocardium and severe sclerosis had been present for a long period before the onset of cardiac symptoms (Weiss et al., 1943). In polyarteritis one or more of the systems may be involved, and cases may present as nephritis, hypertension, bronchial asthma, obscure abdominal pain, peripheral neuritis, and myocarditis. When obscure cardiopathy is accompanied by any of these manifestations, polyarteritis should be considered.

Parasitic infestations such as ascariasis and tropical eosinophilia are common in the tropics. The eosinophil counts in our cases were within normal limits. Löffler (1936) reported two cases and Mümme (1940) one, where eosinophilia was found together with fibrosis of the myocardium. No good evidence incriminating virus infection has yet been produced, though virus myocarditis has been reported from Africa.

Though the gross pathological changes in these cases bear a resemblance to those of congenital fibro-elastosis, the two conditions are entirely different. As mentioned earlier the latter is a developmental defect and, if this was related to the adult disease, cases would be met with in older children, but few such cases have been reported. In isolated myocarditis the endocardium and valves are not involved but mural thrombi and embolic phenomena are common.

The conclusion that can be drawn from this conflicting evidence is that we do not know the essential cause of endomyocardial fibrosis but that certain contributing factors appear to be of importance. A background of malnutrition probably favours the onset and the trigger mechanism that initiates the attack may be a virus infection.

**Pathology**

In all three cases the hearts were hypertrophied and their chambers dilated. Their pericardia were normal. The venae cavea showed dilatation. The coronary arteries showed no pathological changes and their orifices were patent. The cardiac valves were normal. Ante-mortem thrombi were seen in the right atrium in one case and in the crypts of the ventricles. The endocardium of the left ventricle showed more white fibrotic patches towards its apex than did the right. The cardiac muscle, brownish in colour, was generally firm and in one case imparted a grating sensation to the knife. There was endocardial and subendocardial fibrosis (Fig. 3) which was extensive and associated with degeneration of the muscle fibres, hyaline change, and interstitial oedema. There was no cellular infiltration except in relation to organizing mural thrombi (Fig. 4). An organized thrombus was seen in one of the arterio-luminal vessels (Fig. 5). There were thin-walled vessels in the fibrous layer.

Associated necropsy findings included thrombophlebitis of the internal jugular vein (Case 1) and chronic pyelonephritis (Case 3). Additional significant findings included passive congestion of the liver and spleen, and multiple infarcts in the lung with oedema and effusion.
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Fig. 3.—Shows (A) myocardial fibrosis; (B) degeneration and atrophy of the muscle fibres. Haematoxylin and eosin. Magnification, ×110.

Fig. 4.—Mural thrombus in the process of being organized. (A) mural thrombus; (B) cellular infiltration. Haematoxylin and eosin. Magnification, ×48.
PATHOGENESIS

According to Davies and Ball (1955) fibrosis appears in the subendocardium. It then spreads into the endocardium, following thrombosis and occlusion of the arterio-luminal vessels and the Thebesian veins, leading to stasis and ischaemia of the underlying musculature. There is no satisfactory explanation for the initiation of the process. Williams et al. (1954) suggest the possibility of a virus infection, either by itself or with some other contributing factor, initiating the fibro-thrombosis or thrombo-fibrosis. Mural thrombi form on the abnormal endocardium which becomes organized with migration of the adjacent endothelial cells from the edges of the lesion covering the deposit. This is followed later by the appearance of fibroblasts derived from the resting connective tissue cells, a process very similar to wound healing. Myocardial changes are mainly confined to the layers immediately beneath the endocardium. The histological findings of atrophy and fibrosis are consistent with this idea. The thick rigid endocardium may interfere mechanically with the heart's action leading to the hypertrophy, cardiac dilatation, and heart failure (Prior and Wyatt, 1950).

CLINICAL SYMPTOMS AND FINDINGS

All three cases were comparatively young, their ages being 23, 25, and 37 respectively. Their nutrition was poor. There was progressive dyspnea on exertion till the patients were totally incapacitated. There were manifestations of congestive heart failure. The heart was enlarged and a loud murmur was heard in the mitral area and often a triple rhythm.

Cases 1 and 2 were diagnosed as congestive heart failure complicating mitral stenosis. This was due to a doubtful presystolic murmur heard at the apex and left atrial enlargement with a prominent pulmonary conus on screening, but at autopsy there was no disease of the valves. Often mitral regurgitation and occasionally stenosis follows, due to the spread of fibrous tissue to the
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papillary muscles, chordae, and cusps of the mitral valve. Constrictive pericarditis without calcification is often diagnosed in cases of endomyocardial fibrosis. The haemodynamics are somewhat similar, for diastolic filling may be restricted due to the involvement of the myocardium and an inspection of the pericardium at thoracotomy may be the only diagnostic method of choice so that pericardectomy may be performed if constriction is present. In Case 3, though the heart was enlarged, a mistaken diagnosis of constrictive pericarditis could have been partly due to involvement of the myocardium and partly due to a Bernheim effect, as the left ventricle was hypertrophied and this probably interfered with the capacity of the right ventricle, giving rise to a "right-sided constrictive pericarditis". Another feature in two of our cases was the embolic lesions in the lung resulting from the presence of mural thrombi. The only other significant lesion was the hypertension in one case which was probably due to the chronic pyelonephritis.

SUMMARY

Three cases of cardiac enlargement associated with congestive heart failure due to endomyocardial fibrosis are described. At necropsy the most striking pathological features were hypertrophy and dilatation of the heart, with fibrosis of the endocardium and underlying myocardium and associated mural thrombi. There were no significant extracardiac pathological changes except for embolic phenomena in two cases.

The aetiology remains unknown and the pathogenesis is speculative. A brief discussion of the possible aetiology is presented. The differential diagnosis includes any general cardiac enlargement of uncertain origin, heart failure from rheumatic carditis, or any other obscure cardiopathy.

We wish to thank Professor W. A. E. Karunaratna, Drs. W. D. Ratnavale and R. P. Jayawardana for their advice and criticism, Dr. H. Gunawardana for Case 3 and the Superintendent of the Columbo Group of Hospitals, Columbo, for permission to publish this paper.

REFERENCES

Mümme (1940). As quoted by Davies and Ball (1955).