

# Endomyocardial Fibrosis at Autopsy in Cape Town

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## SUMMARY

The pathology of 3 cases of endomyocardial fibrosis (EMF) encountered at autopsy in Cape Town is described. The first case of EMF in a non-White permanent resident of South Africa is documented. The macroscopic features allow distinction between EMF and the usual form of idiopathic cardiomyopathy seen in Cape Town. There is a small potential reservoir of patients in Cape Town with typical EMF, but the presence of a coexistent (valvular) lesion may lead to such hearts being ignored in studies of idiopathic cardiomyopathy.

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Cardiomyopathy of unknown aetiology is not uncommonly encountered at autopsy in Cape Town. The usual case corresponds morphologically to the forms of cardiomyopathy previously reported from South Africa by Gillanders<sup>1</sup> and Higginson *et al.*,<sup>2</sup> and the examples of acute endomyocardial disease with mural thrombi and endomyocardial fibrosis with and without mural thrombi described by Becker.<sup>3</sup> Such hearts often show generalised myocardial hypertrophy and dilatation, and one commonly finds antemortem mural thrombi near the ventricular apices and in the atrial appendages. Endocardial fibrosis, if present at all, is minimal and usually confined to the region of organisation of mural thrombi. The left ventricle is mainly involved (either focally or diffusely), but there is no predilection for the inflow portion of the ventricle, as is characteristic of endomyocardial fibrosis (EMF) of the type described from East<sup>4-8</sup> and West Africa.<sup>9</sup>

The published proceedings of a seminar held at the University of the Witwatersrand in 1957<sup>10</sup> indicate that there are two forms of idiopathic heart disease in Africa. Firstly, there is the South African form as reported by Gillanders<sup>1</sup> and Higginson *et al.*,<sup>2</sup> and secondly, there is endomyocardial fibrosis of the Davies type.

The first case of EMF of the Davies type was reported from South Africa in 1966.<sup>11</sup> The clinical features of 2 patients (cases 1 and 2) of the present report have been documented.<sup>12</sup> The above 3 patients were all White. The rarity of this form of cardiomyopathy in Cape Town (and evidently in South Africa) stimulates us to describe the

pathology of the cases at our disposal. The present report is the first to document endomyocardial fibrosis of the Davies type in a non-White permanent resident of South Africa (our case 3).

## CASE HISTORIES

### Case 1

This 45-year-old White female lived in Zambia most of her life before moving to South Africa in 1962. Symptoms of cardiac failure had appeared in 1960 and she was totally incapacitated by 1963. Cardiac catheterisation and cine angiography showed pulmonary hypertension and a filling defect at the left ventricular apex. Biopsy of the latter was attempted and histology showed scanty collagenous tissue and blood clot. The patient died in 1967, shortly after falling and fracturing her femur.

The heart which was sent to us for examination weighed 450 g and had a normal external appearance apart from its increased size. The coronary arteries and their ostia were fully patent and only very slight atherosclerosis was present. The left ventricle had a maximal free wall thickness of 30 mm, and its cavity was much reduced by massive concentric hypertrophy and marked fibrous endocardial thickening, which was 7 mm thick in areas (Fig. 1). Endocardial fibrosis had obliterated the apex of the left ventricle. No antemortem thrombi were present in the heart. From the apical region the endocardial fibrosis extended

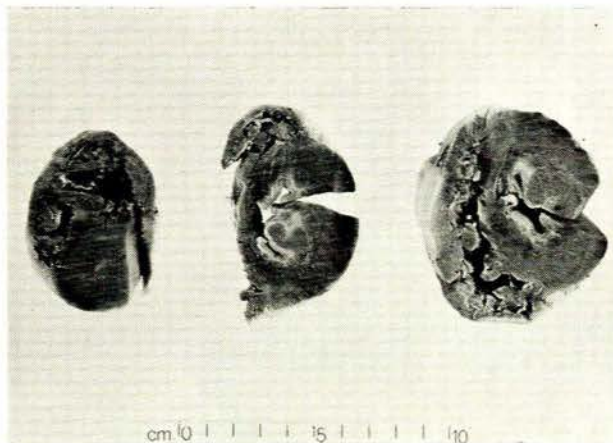


Fig. 1. Case 1. Transverse sections of the heart passing from apex towards the base are seen from left to right. The dense fibrous endocardial thickening envelops the papillary muscles.

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proximally to ensheath the papillary muscles. The mitral valve leaflets were normal, but the distal ends of the chordae were becoming incorporated into the endocardial fibrosis over the papillary muscles. The other heart valves showed no abnormality apart from the aortic valve which had a 2-mm circular defect near the base of its right coronary cusp. This may have been a result of the attempted endomyocardial biopsy procedure. The right ventricle and both atria were dilated and the right ventricular free wall was 10 mm thick. A small patch of endocardial sclerosis was seen on the posterior wall of the right ventricle.



**Fig. 2.** Case 1. Section of left ventricle showing fibrous endocardial thickening, myocardial scarring and a few thick-walled arteries (elastic van Gieson  $\times 96$ ).

Histological examination (Fig. 2) of the left ventricular endocardium showed relatively acellular, hyalinised collagen, which was continuous with areas of fibrosis in the underlying myocardium. The deep portions of the thickened endocardium contained some capillaries together with scanty inflammatory cells (lymphocytes, mast cells, polymorphonuclear leucocytes and plasma cells) and elastin fibres. A few foci of calcification were also present. No excess of acid mucopolysaccharide was observed. A microscopic layer of fibrin thrombus was present on the thickened endocardial surface in areas. The myofibres were hypertrophied and some interstitial oedema was present. Occasional myofibres showed perinuclear vacuolation which did not stain for glycogen. The capillaries were not dilated. Stellate areas of fibrous replacement of the left ventricular myocardium were present, the largest occupying one high-power field. In such areas the small arteries were thick-walled, mainly owing to intimal fibroplasia which was eccentric in some instances. A few small arteries contained organising thrombo-emboli. The pathological diagnosis was endomyocardial fibrosis of the Davies type.

### Case 2

A 55-year-old White female had contracted Loa-loa while living in the Belgian Congo during World War II.

She had pneumonia at about the same time and thereafter suffered recurrent respiratory infections. Symptoms of cardiac failure first appeared in 1969 and led to repeated hospital admissions. Murmurs of mitral and tricuspid incompetence and a loud apical gallop were present. Left ventricular angiography revealed a moderately enlarged ventricular cavity with apical obliteration. An endocardial biopsy taken with the Konno biotome from the apex of the right ventricle revealed hypertrophied myofibres only. She slowly deteriorated and died in hospital in early 1972.

At autopsy, apart from bilateral bronchopneumonia, the pathological findings of note were confined to the heart, which weighed 675 g. All four cardiac chambers were dilated and hypertrophied. The coronary arteries had minimal atheroma. Towards the apex of the left ventricle the endocardium was thickened by dense fibrous tissue, contraction of which had drawn the bases of the papillary muscles into apposition (Fig. 3). A thin layer of thrombus was present on the surface. The fibrous layer enveloped the small anterolateral papillary muscle. The remainder of the left ventricular endocardium, including that behind the posterior mitral leaflet, was normal. While some mitral chordae were slightly thickened, all appeared freely mobile and were not adherent to endocardium at any site. Two small areas of endocardial thickening (the larger 2 cm in diameter) were present in the right ventricle, one on the anterior wall and the other on the septum.



**Fig. 3.** Case 2. Endomyocardial fibrosis of left ventricle with apposition of papillary muscles and unorganised surface thrombus.

Histology of the endocardial lesion showed a thick layer of acellular fibrous tissue, the deeper portions of which were still vascularised. The underlying myocardium was not significantly fibrosed, but did show mild intra- and intercellular oedema, with irregular myofibre hypertrophy. No Aschoff bodies were present and the intramyocardial arteries were normal. The pathological features in this heart conformed to descriptions of endomyocardial fibrosis of the Davies type.

### Case 3

The third patient was a 49-year-old chronic alcoholic Cape Coloured man, who had lived his entire life in the Cape Province of South Africa. Heart failure had been present for 2 years before his death. There was no history of ischaemic heart disease and his blood pressure had been normal on all occasions. At one stage he had had an alcoholic peripheral neuritis. Fainting attacks were attributed to severe bradycardia, and later other arrhythmias developed. He was admitted to hospital in cardiac failure in March 1972 and a transvenous pacemaker catheter was inserted into the right ventricle. Death was due to cerebral embolism.

The patient was well-built and had mild peripheral oedema at autopsy. The lungs were oedematous and pulmonary artery atheroma reflected his pulmonary hypertension. The heart weighed 535 g and the left ventricular free wall was 22 mm thick. Endocardial fibrous plaques were present on the anterior wall of the left ventricle and behind the posterior mitral leaflet. At both sites the endocardial fibrosis measured up to 4 mm in thickness. While the mitral valve showed no intrinsic abnormality, several of the chordae of its posterior leaflet were bound down to the underlying endocardium throughout their length, leading to valvular incompetence. The left atrial appendage contained globular antemortem thrombi. The right ventricle was hypertrophied and dilated, and showed endocardial sclerosis of its septal wall. Some of the chordae of the septal leaflet of the tricuspid valve were firmly bound down to the underlying fibrosed endocardium (Fig. 4), with resultant valvular incompetence. The pulmonary and aortic valves were normal. A few thrombi were present in the right atrial appendage. The coronary arteries showed moderate atherosclerosis without any significant reduction in luminal cross-section.

Microscopically the endocardial lesions consisted of dense collagenous tissue with scanty elastin. The myocardium showed an extraordinary degree of fibrosis (Fig. 5)



Fig. 4. Case 3. Endocardial thickening on the septal wall of the right ventricle, with adherent tricuspid valve chordae. A small patch of endocardial sclerosis is also present on the free wall.

throughout all the sections examined. Some myofibres were hypertrophied whereas others looked atrophic. There were no acute myocardial changes. Several of the intramyocardial arteries had thick walls due to intimal fibrosis and medial hypertrophy. Other autopsy findings included cardiac cirrhosis of the liver, fibrous thickening of the splenic capsule and a massive right-sided cerebral haemorrhage. The cardiac changes were those of endomyocardial fibrosis of the Davies type.

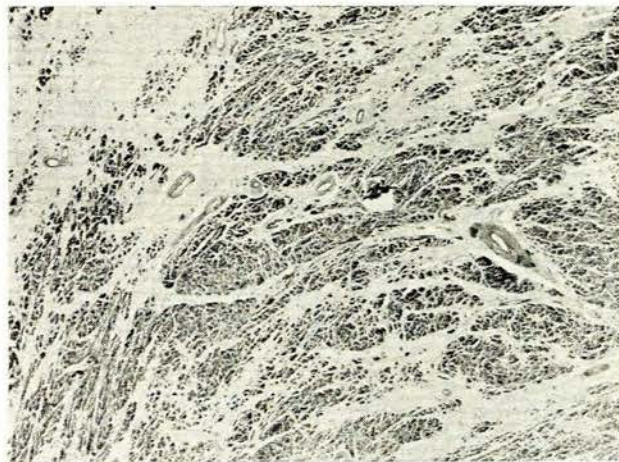


Fig. 5. Case 3. Section of left ventricular myocardium showing severe degree of diffuse fibrosis (H. and E.  $\times 96$ ).

### DISCUSSION

Case 3 is unique since all the other cases of endomyocardial fibrosis hitherto reported from South Africa have been Whites who have lived part of their lives in tropical Africa.<sup>21-23</sup> Our third patient was a Cape Coloured male who had never left South Africa. Hitherto, the finding of EMF solely in Whites who had visited the tropics has been used by some as circumstantial evidence that EMF is a separate entity from congestive cardiomyopathy. While our patient with EMF would tend to diminish the effectiveness of this argument, we have not in our experience encountered forms of cardiomyopathy having a macroscopic appearance intermediate between congestive cardiomyopathy and classical endomyocardial fibrosis. (The histological appearances are not distinctive.) Nor have we encountered EMF in Black patients we see at autopsy. Thomson<sup>24</sup> felt that the differentiation between EMF and the South African variety of cardiomyopathy was purely arbitrary. McKinney<sup>15</sup> holds a similar viewpoint. Brink and Weber<sup>25</sup> draw a clear distinction between EMF and the usual South African cardiomyopathy.

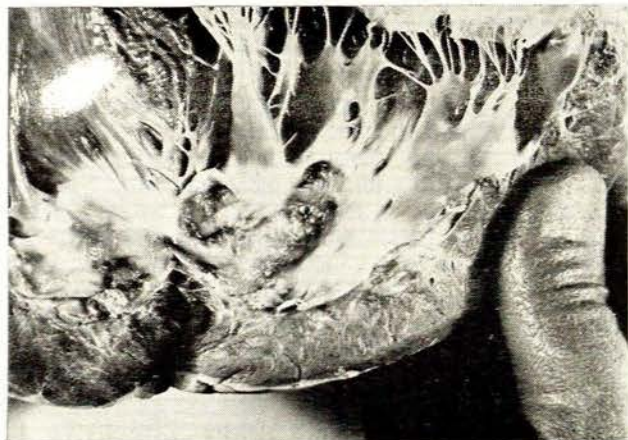
Becker<sup>3</sup> labelled some of his cases endomyocardial fibrosis, but did not indicate how these compared morphologically with those described by Davies. Becker's Fig. 23 illustrates one such case.<sup>3</sup> The inflow tract is relatively spared, endocardial sclerosis is focal and diffuse, with maximal involvement of the outflow tract of the left ventricle. The relationship between congestive cardio-

myopathy (as seen commonly in South Africa) and endomyocardial fibrosis of the Davies type (as seen rarely in South Africa and commonly elsewhere in Africa) is still uncertain. We have encountered 2 additional patients with obscure endocardial lesions who are relevant to the present discussion.

**Case 4** was a 43-year-old Black male labourer who had lived in Cape Town for an unknown number of years. Symptoms of cardiac decompensation were first noted in 1956. He continued working until 1961 when he died of a cerebral embolus. Physical examination shortly before death showed aortic systolic and diastolic murmurs, but no cardiac failure. No past blood pressure readings were available.

At autopsy the body was that of a muscular man without signs of malnutrition. Oedema was absent. The lungs showed moderate silico-anthraxosis, healed tuberculosis and pulmonary artery atheroma. The heart weighed 644 g and showed hypertrophy of all its chambers, most marked in the left ventricle, which was 30 mm thick. The aortic valve showed fusion of its commissures and calcification of its cusps, leading to stenosis and incompetence. The pulmonary, mitral and tricuspid valves were normal. A small valve pocket was present on the septum just below the aortic valve. The endocardium at the apex of the left ventricle showed a striking degree of fibrous thickening, 6 × 2 cm in extent and up to 3 mm thick (Fig. 6). This fibrous tissue extended proximally to involve the bases of the papillary muscles and the lower part of the inter-ventricular septum. Some surface thrombus was also present. The underlying myocardium appeared normal. A small area of right ventricular endocardial thickening was present towards the apex. The coronary arteries were free of atheroma; the aorta showed fatty streaking and early atheroma. Death was due to a massive right-sided intracerebral haemorrhage.

Histology showed scattered areas of fibrosis in the left ventricle, much less severe than that seen in case 3. The endocardial plaque in the left ventricle consisted of



**Fig. 6.** Additional case 4. Endomyocardial fibrosis in a patient with a coexistent aortic valve lesion. Such cases tend to be ignored in studies of idiopathic cardiomyopathy.

dense hyalinised collagen, with areas of calcification and some deposits of haemosiderin together with scanty plasma cells. The pathological findings in this heart were those of endomyocardial fibrosis with associated aortic nodular sclerosis.

Case 4 serves to indicate that there is a small potential reservoir of patients in Cape Town with typical endomyocardial fibrosis, but the presence of a coexistent (valvular) lesion may lead to such hearts being ignored in studies of idiopathic cardiomyopathy. The occurrence from time to time of endomyocardial fibrosis and some other unrelated cardiac lesion is not unexpected. At present such a situation leads to the cardiomyopathy being overlooked, since idiopathic cardiomyopathy is diagnosed by exclusion of all other disease processes.

**Case 5.** This 61-year-old White male developed cardiac failure of acute onset. The cardiac failure became so severe and unresponsive to therapy that 2 years after the first onset of symptoms cardiac transplantation was performed as a last resort. The patient died of cardiac rejection and bronchopneumonia 13 days after transplantation. The patient's original heart (removed at the time of transplantation) weighed 580 g. There was no sign of infarction and the myocardium appeared translucent, with some mottling. The coronary arteries were remarkably free of atheroma. All four cardiac chambers were dilated and hypertrophied. The left ventricular endocardium bore multiple pearly-white plaques of fibrous tissue having the appearance of organised thrombi (Fig. 7). The distribution was unlike that of endomyocardial fibrosis of the Davies type. No fresh antemortem thrombi were seen and the heart valves were normal.



**Fig. 7.** Additional case 5. Multiple plaques of endocardial fibrosis in the left ventricle. The appearance is unlike that of endomyocardial fibrosis of the Davies type.

Endocardial thickening and fibrosis corresponding to the plaques was observed microscopically. The fibrous tissue was cellular in areas and contained scanty lymphocytes. Fibrous replacement of the superficial myocardium and obliteration of Thebesian vessels were additional features.

An increase of fine elastic fibres accompanied the fibrosis. The myocardial fibres were generally increased in size and showed intracytoplasmic oedema with perinuclear vacuolation. The nuclei were large, of variable size and often bizarre in appearance. There was interstitial oedema and the capillaries were dilated. The appearance was that of idiopathic cardiomyopathy with endomyocardial fibrosis. While not conforming to the classical picture of endomyocardial fibrosis as described by Davies and colleagues, we are including it here for completeness as this case is also unique in our experience. By including these 2 additional cases of cardiomyopathy we are attempting to avoid an arbitrary selection of our cases of cardiomyopathy with endocardial sclerosis.

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