Eosinophilia and endomyocardial fibrosis

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From the earliest days of the study of endomyocardial fibrosis (EMF) in Kampala, its resemblance to Löffler's endocarditis (Löffler, 1936) has been recognized as a possible clue to its aetiology (Williams, Ball & Davies, 1954). This remains a controversial matter and the purpose of this paper is to review the evidence.

Löffler's endocarditis

We have recently completed a review of ninety reported cases of endomyocardial lesions in patients with blood eosinophilia (Brockington & Olsen) and a personal study of the histology of thirty of them. Morphologically there are three variants. There are patients with a long history (average 25 months) who have an extensive area of ventricular endocardial fibrosis, sited in the region of the apex and inflow tract, submerging the trabecular pattern and encroaching on the papillary muscles, and often sharply demarcated. There are others with a shorter history (average 10 months) and obliteration of a large part of the ventricle by masses of tightly packed thrombus. There are a few who have died within weeks of the onset and been found to have necrosis of the myocardium and infiltration by eosinophils and other leucocytes. Between these extremes there are intermediate forms, and occasionally a patient has shown endocardial fibrosis in one ventricle and a 'global thrombus' in the other.

Twenty-two of these patients have had various types of leukaemic eosinophilia (Roberts, Liegler & Carbone, 1969; Brockington, Luzatto & Osunkoya, 1970). In these patients the eosinophilia cannot be secondary to the heart lesion, nor an irrelevant by-product of a cardiopathic allergic process. The heart lesion seems to be a complication of eosinophilia itself.

EMF in Europeans resident in Africa

Europeans who expose themselves to certain tropical environments are prone to similar endomyocardial lesions. Sixteen cases confirmed by necropsy have so far been reported (Brockington et al., 1967). They have been identified as EMF by British cardiologists and Löffler's endocarditis by their French colleagues. They have been living in Nigeria, Cameroun, Gabon, the Central African Republic and Zaire (but not Uganda). The apparent prevalence is much higher than Löffler's endocardiist in temperate countries, judging from published case reports (which we think legitimate with differences of this magnitude): the sixteen have emerged from a European population of perhaps 150,000 (spending only part of their lives in the area) while in the same 40-year period seventy-eight cases have been reported from 700 million in the home countries. The apparent cause of this increased prevalence is filariasis which has been evident in most of the patients. There are two features which make one certain that Gerbaux, Pannier and other European experts are justified in identifying these lesions as a variant of Löffler's endocarditis. First, most of the patients have had eosinophilia in the blood. Secondly, seven have had a peculiar type of disseminated micro-embolism occurring at the beginning of the illness and leading to central nervous disorders which are on the wane by the time heart failure ensues. This is characteristic, possibly pathognomonic, of Löffler's endocarditis. However, the peak eosinophil counts (average 7000/mm³) are lower than in Löffler's endocarditis (average 32,000/mm³) and the duration of the illness somewhat longer (24 months compared with 19 months) due to the lower proportion of thrombotic lesions. Histologically a tissue eosinophilia was present in only 2/7 patients, and then it was slight (6%, 1%), comparing with 21/29 Löffler's endocarditis (average level 14%). 'EMF in Europeans' is therefore the late fibrotic form of Löffler's endocarditis, with somewhat lower blood and tissue eosinophilia and a higher prevalence apparently due to filariasis.

Davies' endomyocardial fibrosis

Davies' EMF (Davies, 1948), as found in the indigenous people of equatorial Africa, also resembles the fibrotic form of Löffler's endocarditis, and morphologically the only difference is the comparative lack of superficial thrombus. We have compared the histology of sixteen cases of Löffler's endocarditis in the fibrotic stage and nineteen cases of EMF from Nigeria, Uganda and Brazil. Working without knowledge of the country of origin, Olsen was unable to find criteria (either those claimed in the literature or personally devised) which would distinguish the two groups. Both had layered hyaline thickening, with a condensation of elastic tissue, fibrous septa and myocardial fibrosis. The
best differential point was the presence of eosinophils in the intermediate inflammatory zone; they were always present in early cases of Löffler’s endocarditis but were absent in half the fibrotic lesions, and even in one patient with eosinophilic leukaemia. They were usually absent in EMF but were present in 3/9 Nigerian patients, at a considerable level (24%, 48%) in two of them. None of the five Ugandan patients had a tissue eosinophilia, but Davies (1948) reported ‘an intense eosinophil infiltrate of the thrombus and to a lesser extent the myocardium’ in a number of his original series. We are not claiming on the basis of this histological study that this lesion is specific to EMF and Löffler’s endocarditis. That would require an extensive series of controls. But this study has added to a long list of unusual features which they share.

The most important difference between Davies’ EMF and Löffler’s endocarditis is the lack of impressive eosinophilia in African patients. Only 40% of Nigerians with EMF have an eosinophilia of over 1000/mm³ and the average count in nineteen patients (685/mm³), though raised by European standards (Discombe, 1946), is actually lower than in other young cardiac patients, e.g. those with rheumatic heart disease (734/mm³). Since eosinophilia is thought to play an aetiological rôle in Löffler’s endocarditis (Brockington et al., 1970), this is an important negative finding. However, Löffler’s endocarditis is clearly understandable in terms of an initial insult followed by normal healing, and the hypothesis associates eosinophilia with the active stage. It is known that eosinophilia (both in the blood and the endocardial lesion) can peter out during the course of the illness. Its persistence until the time of presentation depends on the stage at which the patients consult. They often present at an early stage, with micro-embolism, or acute myocardial failure, or thrombotic obliteration of the ventricle, or with non-cardiac complications of the severe diseases which produce eosinophilia in temperate countries. But African patients almost always present with chronic cardiac symptoms due to the late effects of endocardial scarring. No eosinophil counts have been made in the early stages.

The persistence of eosinophilia also depends on the natural history of eosinophilia in the underlying diseases (e.g. leukaemia, drug sensitivity, parasitic infections). In Nigerian EMF there is evidence that this is filarial infection (Ive et al., 1967). These infections are associated with a mild but definite eosinophilia, averaging 890/mm³ compared with 420/mm³ in controls (Brockington, 1973). It would fit well with the hypothesis if further research showed that they began with a more severe eosinophilia of short duration. The association of Nigerian EMF with allergic parasitic infections is, in any case, indirect evidence for a link with ‘EMF in Europeans’ and Löffler’s endocarditis.

At this stage the case for the identity of EMF and Löffler’s endocarditis is strong but incomplete. It deserves further investigation because, in these rare but pernicious European lesions, one can observe the early stages of the cardiopathic process.

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References


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