SESSION IV

Chairman: Dr E. G. J. Olsen

A comparison of the clinical and cardiological features of endomyocardial disease in temperate and tropical regions

J. Davies* M.R.C.P.
G. Vijayaraghavan† M.D., D.M.
J. A. De Souza‡ M.D.

*Department of Immunology, Royal Postgraduate Medical School, London, †Medical College Hospital, Trivandrum, Kerala, India and ‡University Hospital, Bahia, Brazil

Summary

This study was designed to compare the clinical and cardiological features of endomyocardial disease in temperate and tropical regions. Eleven patients were studied in the U.K., 47 in India and 8 in Brazil. The patients in the U.K. were older, with a male predominance, and they had a systemic illness: the hypereosinophilic syndrome. Half of these patients presented in the early necrotic stage of the disease, and all had biventricular involvement. On the other hand, patients in the tropical countries were younger, with an equal sex incidence, and were from poor, malnourished communities with heavy parasite loads, especially filariasis in India. None presented in the early necrotic stage of the disease and a quarter had isolated right or left ventricular disease.

In order to account for these differences between patients in temperate and tropical regions with endomyocardial disease, it was proposed that the nature of the underlying disease and the rate at which endomyocardial lesions develop, determine the clinical features of this disorder. In temperate climates eosinophil granule toxins may produce a rapidly progressive form of the disease in patients with the hypereosinophilic syndrome, whereas the disease may take longer to develop in patients in tropical climates, who have a less marked eosinophilia due to parasitic infections.

KEY WORDS: endomyocardial disease, temperate, tropical regions.

Introduction

Tropical endomyocardial disease became widely known after its description in Uganda (Davies, 1948). Subsequent work there clarified the clinical and pathological features of the disorder, and it was classified as a distinct cardiomyopathy (Patel, D’Arbela and Somers, 1977). However, the presence of an eosinophilia in many of these patients, especially those living in areas of endemic filariasis, raised the possibility that tropical endomyocardial disease had a similar pathogenesis to eosinophilic endomyocardial disease, which is mainly seen in temperate climates (Gerbaux et al., 1956; Ive, Willis and Ikeme, 1967). This led Brockington and Olsen (1973) to carry out a review of pathological specimens of late stage (fibrotic) endomyocardial disease which had been recognised in tropical and temperate regions. They found that the lesions were indistinguishable.

During the past 7 years we have been studying patients in the United Kingdom (U.K.) with eosinophilic endomyocardial disease which occurs as one complication of the hypereosinophilic syndrome (Spry et al., 1983). Clinical and experimental studies supported the suggestion that this form of endomyocardial disease was related to the presence of large numbers of eosinophils in the blood, particularly degranulated eosinophils. It is proposed that the granule products from these cells cause the endomyocardial lesions (Spry, Tai and Davies, 1983).

Although it was felt that both tropical and eosinophilic endomyocardial disease could have a similar pathogenesis (Olsen and Spry, 1979), it became necessary to explain why a number of differences had been reported. For this reason it was decided to carry out a study of these forms of endomyocardial disease in the U.K. and tropics, to compare the clinical and cardiological features of endomyocardial disease in these regions. Unfortunately, this could not be done in Uganda, so two
other tropical regions with a high incidence of tropical endomyocardial fibrosis were chosen: Kerala (South India) and Bahia (Brazil).

Patients

The 11 patients in the U.K. with eosinophilic endomyocardial disease have been described previously (Davies et al., 1983). They all had biventricular endomyocardial disease. Nine had marked mitral valve disease, and 6 had severe tricuspid regurgitation. Four patients were studied during the early necrotic stage of the disease, and 5 were studied in the late fibrotic stage.

Forty-seven patients were studied in India and 8 patients in Brazil. These patients all had clinical and cardiological features of advanced endomyocardial disease in the late fibrotic stage.

Results

A summary of the general and cardiovascular features of patients with endomyocardial disease in the temperate region and the two tropical regions is shown in Fig. 1 and 2.

A number of important differences were found. Many patients living in the U.K. were in their fourth decade (mean age 38 years) and 9 were male. Half of them presented in the early necrotic stage of the disease. They all had a systemic illness with hypereosinophilia, the hypereosinophilic syndrome. This syndrome is associated with wide-spread tissue injury (Spry, 1982) including the heart (eosinophilic endomyocardial disease), skin, retina (Chaine et al., 1982), blood vessels, lymph nodes, spleen, gastrointestinal tract and lungs. On the other hand, patients in the tropical regions were younger (mean age 17 years in India and 30 years in Brazil), and had an equal sex incidence of the disease. They were from the poorest socio-economic groups, with malnutrition and features of chronic growth retardation. They all presented at a late stage of the disease with ascites and/or periorbital oedema. Despite clinical features of advanced cardiac disease, they were remarkably free from severe symptoms, and appeared to have adapted to their restrictive heart failure. This suggested that heart disease had been present for many years. None of them had suffered from a systemic illness with similarities to the hypereosinophilic syndrome.

Cardiological studies showed some similarities and some differences in the clinical features of patients with endomyocardial disease from the U.K. and the tropics. Most patients had a loud third heart sound and raised jugular venous pressure. A positive Kussmaul's sign was noted frequently in both groups. However, murmurs of atrio-ventricular valve regur-

![Fig. 1. Comparison of the general clinical features of patients with endomyocardial disease in the U.K. and in India and Brazil. Striking differences are shown which suggest that patients in temperate regions have a more aggressive and rapidly progressive disorder than patients in tropical regions.](http://pmj.bmj.com/)
Endomyocardial disease: regional differences

United Kingdom
- Presentation:
  - Late stage 50%
  - Early stage 50%
- Patients have a systemic illness
- Emboli/thrombi common
- Biventricular disease 100%
- ECG: Sinus rhythm, ST depression
- Murmurs of mitral disease common

India and Brazil
- Presentation:
  - Late stage 100%
- No evidence for a systemic illness
- Emboli/thrombi rare
- Biventricular disease 75%
- Isolated right ventricular disease 20%
- Isolated left ventricular disease 5%
- ECG: Atrial fibrillation, right axis deviation
- Murmurs of mitral disease rare

- The pathology of late stage disease is identical in both regions

Fig. 2. Comparison of the cardiovascular disease in patients with endomyocardial disease in the U.K. and in India and Brazil. The cardiological features showed many similarities. Differences were largely related to variations in the staging of the disease at diagnosis, and the extent of involvement of right and/or left ventricles. (ECG = electrocardiogram)

Fig. 3. Electrocardiogram of a man in the U.K. with eosinophilic endomyocardial disease, showing sinus rhythm with widespread ST segment and T wave changes.

gitation, particularly mitral regurgitation, were more common in patients in the U.K.; half of the patients in India and Brazil had no cardiac murmurs, even though they all had severe restrictive heart defects. Electrocardiograms showed some differences: in the U.K. there was sinus rhythm with ST depression (Fig. 3), whereas in India and Brazil atrial fibrillation with right axis deviation was common (Fig. 4).

Echocardiography showed no significant differences between the 2 groups of patients, when staging of the disease was taken into account. Details of the echocardiographic features of eosinophilic endomyocardial disease have already been published (Davies et al., 1982). M-mode echocardiography showed non-specific changes which did not correlate either with the severity of endomyocardial disease or the thickness of the posterior left ventricular wall. On the other hand, two-dimensional echocardiography, and regional echo amplitude analysis, showed abnormalities corresponding to areas of endomyocardial disease.

Results of haematological studies and immunoglobulin measurements in patients with eosinophilic endomyocardial disease in the U.K., have been
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(Spry et al., 1983). The principal
findings were that patients had markedly raised
blood eosinophil counts, and that many of the
eosinophils were degranulated. Three patients had
high levels of serum IgM and IgE. Similar measures-
ments in patients in India and Brazil were com-
licated by the common occurrence of parasitic infec-
tions in these areas. For this reason, comparisons
were made in India between 28 patients with tropical
endomyocardial disease, and age and sex matched
control subjects. These showed that patients with
tropical endomyocardial disease had blood eosino-
phil counts that were no higher than those in the
control subjects. An important difference between
these patients and those in the U.K. was that no
degranulated eosinophils were found in their per-
ipheral blood. The patients in India, and their
controls, had raised immunoglobulin levels, but a
higher proportion of the patients had markedly
raised serum IgG, IgA, IgM and IgE. A larger
number of patients in India had raised filarial
antibody titres compared to controls.

Discussion
Although there is no pathological difference be-
tween late stage fibrotic endomyocardial disease in
temperate and tropical climates (Brockington and
Olsen, 1973), this study has clearly shown some
important regional differences in the clinical pre-
sentation, cardiological features and laboratory abnor-
malities. The principal differences were in the sex
incidence and age groups affected, and the absence of
isolated left or right ventricular disease in the U.K.
However, these studies show no fundamental differ-
ences in the nature or characteristics of endomyocar-
dial disease as it affected the heart in either region.
For this reason, these differences probably indicate
variations in the underlying disease process, which
leads to a final common cardiac pathology.
Patients in the U.K. all had one underlying disease:
the hypereosinophilic syndrome. This did not appear
to have been present in any of the patients studied in
India or Brazil, and none had a preceding history
suggesting that they had some variant of this
syndrome. However, as there is strong clinical and
experimental evidence to suggest that eosinophils
themselves are involved in the development of
eosinophilic endomyocardial disease (Spry, Tai and
Davies, 1983), it is important to consider whether
eosinophils might also have been involved in the
development of tropical endomyocardial disease.
Most of the Indian and Brazilian patients had an
eosinophilia, even though they were in the late
fibrotic stage of the disease. They came from poor
socio-economic groups and had a higher incidence of
parasitic diseases. The close association of endemic
filariasis with tropical endomyocardial disease in
South India is unlikely to be accidental. Patients with
tropical endomyocardial disease in this area had
higher filarial antibody levels than controls, suggest-
ing that they may have had repeated or more severe
infections than controls who did not develop this
disease. There does not appear to be an association of
tropical endomyocardial disease in Brazil with a
single parasitic disease.

It is possible to explain a number of the differences
between eosinophilic endomyocardial disease, in
temperate and tropical regions, by taking into ac-
count the nature of the underlying disease process. In
temperate climates the hypereosinophilic syndrome,
which is the principal cause for eosinophilic endomy-
occardial disease, is a severe disorder leading to early presentation, episodes of acute endocarditis and rapid progression, over several months, to the late fibrotic lesions. On the other hand, in the tropics, parasites are the principal cause of an eosinophilia, which is so common that little attention is paid, unless the patient is unwell. Occasionally hypereosinophilia develops, as in tropical (filarial) eosinophilia (Spry and Kumaraswami, 1982). Most clinical problems associated with parasitic infections occur during childhood, when there is the highest incidence of infection, and adults usually have some degree of immunity or tolerance to their chronic parasite load. If eosinophil derived toxins are responsible for the development of tropical endomyocardial disease, this is likely to develop in a younger age group, over a more prolonged period, than in temperate climates where older male patients with the hypereosinophilic syndrome are most at risk from developing this disease. In the later stages of eosinophilic endomyocardial disease, the peripheral blood eosinophilia may decline or disappear. This may also occur in tropical endomyocardial disease, accounting for the normal blood eosinophil counts in a small proportion of these patients. This possibility emphasises the importance of detecting tropical endomyocardial disease in its early stages, so that a search can be made for possible underlying eosinophilic disorders. As many of these respond well to treatment, it may be possible to prevent progression of tropical endomyocardial disease to its late stages.

It is concluded that, although a number of clinical and cardiological features of endomyocardial disease were found to be different in a temperate and two tropical regions, there were many similarities between them. For this reason we propose that they have a common pathogenesis linked to underlying eosinophilic disorders. It is suggested that differences are related to the various causes of eosinophilia in these regions, and the rate at which eosinophil granule toxins induce cardiac damage. It is therefore important to find methods for detecting tropical endomyocardial disease in its early stages before severe and life threatening damage has occurred.

Acknowledgments

This project is being supported by the Wellcome Trust and British Heart Foundation, and forms part of a multicentre project on endomyocardial disease which is being carried out under the auspices of the International Society and Federation of Cardiology. We are particularly grateful to Professor J.G. Goodwin, Dr Celia Oakley, Dr E.G.J. Olsen and Dr Bridget Ogilvie in London, Dr D.V. Nair and Dr George Jacob in Kottayam, Kerala, Dr S. Sadanandan and Dr Ramachambaram in Trivandrum and Professor Guimaraes in Bahia, Brazil for their advice and help in setting up this project. Further details of the clinical features and investigations in the patients reviewed here will be provided later in joint publications.

References


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doi: 10.1136/pgmj.59.689.179

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