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Discussion

DR A. O. FALASE: Eosinophilia is very common in Africa, but what is hypereosinophilia? It needs to be defined. Does hypereosinophilia, either mild or moderate, always occur in association with endomyocardial fibrosis? Is it the degranulation and not necessarily the hypereosinophilia that is responsible? I think it is possible that you might get degranulation without hypereosinophilia and, do normal people have degranulated eosinophils? Finally, may I suggest that it is possible that endomyocardial fibrosis is the end result of a variety of factors, as is constrictive pericarditis.

DR OLSEN: In our own cases with eosinophilia, as well as those in the literature, there is no absolute number in which endomyocardial disease occurs and below which it does not occur. I have already mentioned that there are well described cases of endomyocardial fibrosis where there has never been an associated eosinophilia. Many of these patients have not been examined specifically for degranulation, but I suspect that these patients had a significant number of degranulated cells. In the hypereosinophilic syndrome, a variety of target organs such as the lung are involved but degranulation of eosinophils has not been documented and the heart is not usually affected. Therefore, as far as our knowledge extends, it is particularly the significant number of degranulated cells which are important in the associated endomyocardial disease. With regard to the causes of fibrosis, I have never seen any endocardial changes suggestive of endomyocardial fibrosis as we have defined it today. I do not believe it is a totally non-specific reaction occurring as a result of organising thrombi. In my experience of patients with myocardial infarction and other conditions where the endocardium is damaged, thrombus is superimposed, but organisation along uniform lines occurs, ending in a fibro-elastic plaque. The layering which is so characteristic of endomyocardial fibrosis is not seen. In the carcinoid syndrome, a normal endocardium is preserved, upon which gelatinous material associated with this particular disease process is superimposed. Furthermore, the histological features are totally different, elastic tissue and dense collagen tissue is never seen but there is an increase in acid mucopolysaccharides. Collagenosis has been described by Becker, Chetidakis and Van Lingen (1953) in South Africa, but this is different, probably non-specific degenerative change.

DR J. J. PUIGBO: I would like to know if cases with a combination of a normal eosinophil count, degranulation and endocardial lesions have been described.

DR OLSEN: No, degranulation has not been studied in cases of endomyocardial disease with normal eosinophil counts.

DR P. J. RICHARDSON: Clearly there must be many patients in whom eosinophilia is present but without endomyocardial disease. Is there a genetic factor predisposing to that immune response?

DR OLSEN: Yes, this will be dealt with in detail later, but we know, for example, that eosinophils have an affinity for IgG and C_3b and an unmasking of Fc receptors can happen as a result of a variety of stimuli such as parasites and other infections (Olsen and Spry, 1979). I would like to say again, eosinophilia in itself is not the important factor, it is the significant number of abnormal (degranulated) cells that is important which affect the heart as the target organ. Why the heart should be the target organ, I don't know and nobody else does. I would even like to go so far as to suggest that there is now ample evidence, sparse though it may be in some parts of the world, that an association with degranulated eosinophils has been found. By definition cardiomyopathies are defined as heart muscle disease of unknown causes. In other conditions, for example, neuromuscular disorders, we know of the association, but we do not know the mechanism of cardiac involvement. We know that alcohol has a direct effect on the myocardium, but not the precise mechanism. We exclude these disease entities from cardiomyopathies and categorise them under specific heart muscle disease. Is it not time for us to consider that restrictive cardiomyopathy, as I have presented it today, should be removed from cardiomyopathies and re-classified under specific heart muscle disease? I think almost everyone is now in agreement that EMF and Löffler's disease are the same thing. Several different stimuli may be present in different parts of the world culminating in degranulated eosinophils.

CHAIRMAN: I suggest that we are tending to neglect the possibility of an additional factor and, of course, the relation of two variables is an epidemiologist's nightmare. I would like again to sound a note of warning that, even though pathologically and clinically these diseases are extremely similar, even identical, this does not alter the fact that there may be other factors which are responsible both for the degranulation of the eosinophil and for endomyocardial fibrosis. I do not think we have got to the point yet where we can quite say that we know the cause of endomyocardial fibrosis.

DR OLSEN: We do not know the cause, but is it not exactly the same as Duchenne muscular dystrophy where we know heart involvement occurs. Despite many factors the final common pathway is degranulated eosinophils.

DR H-D. BOLTE: I should like to come back to the morphology and the three stages you defined. You say the acute is necrotic, the next stage is the thrombotic stage and the third the fibrotic. How can you be sure that the stages correlate to the time of follow-up. How do you know that a patient who is at one point in the necrotic stage will have the fibrotic stage later on.

DR OLSEN: The findings leading us to suggest that the changes are sequential were a retrospective study (Brockington and Olsen, 1973). The onset of clinical symptoms and time of death was recorded. In each group the disease

had lasted for several months, but the average duration where we saw a myocarditis and early necrotic changes without significant endocardial thickening was 5·5 weeks. The same applied to the other groups (thrombotic phase 10 months, fibrotic 24·5 months).

There appear to be stages according to the length of history. Furthermore, subsequent work on endomyocardial biopsy tissue obtained by bioptome has shown that the necrotic and thrombotic phases are sequential. We have not found a thrombotic stage changing subsequently to a fibrotic stage. The latter phase is, for technical reasons, often difficult to obtain by bioptome, but subsequent post-mortem examination has confirmed that the fibrotic stage was present. There are however isolated cases where sequential changes do not occur.

DR PUIGBO: Dr Olsen, do you think from the description of the thrombotic and necrotic stages that there is some intermediary stage? We have observed a patient with mitral insufficiency and a blunt apex on the angiogram indicating EMF. The biopsy showed a severe myocarditis of the eosinophilic type and we supposed that these stages were superimposed.

DR OLSEN: We have reported 5 stages (Brockington and Olsen, 1973). There is a lot of overlap and gradation, but you can roughly separate the pathology into the 3 major groups.

DR C. J. F. SPRY: Have different stages of the disease been recognised in different parts of the same heart?

DR OLSEN: Yes, we have found that as well. Usually in the fibrotic stage we found no other stage, but we frequently have seen necrotic changes in one part and the thrombotic stage in another.

References

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Notes