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# ENDOMYOCARDIAL FIBROSIS IN A LABORATORY RAT

Anilkumar T.V.[1], Vineetha V.P.[2], Thulaseedharan N.K.[3] and Harikrishnan V.S.[4]
*Sree Chitra Tirunal Institute for Medical Science and Technology*

Endomyocardial fibrosis (EMF) affecting heart, although rare in animals, has been reported in domestic (Maxie and Robinson, 2007) as well as laboratory animals (Frith et al., 1977). It is essentially a non-infectious disease of public health and demographic significance which is prevalent in African, Tropical Asian and American countries characterised by variable extent of fibrosis of the endocardium and myocardium (Bukhman et al. 2008). The incidence of EMF is high in India, especially in its southern state, Kerala (Kumar et al., 1996). It is linked to dietary habits, high parasitic load (tropical eosinophilia) and environmental factors. In spite of its high prevalence among humans, cases of endomyocardial fibrosis have not been reported in any animal species in India. This report documents endomyocardial lesions observed at histopathology performed as part of routine post-mortem investigation in a laboratory animal colony of Wistar rats where the animal care guidelines follows ISO platform (ISO 10993 Part-II). The Wistar colony is a random bred, open colony which was established thirty years back with breeding nucleus procured from National Institute for Nutrition, National Centre for Laboratory Animal Science, Hyderabad, India. The breeders are replaced once in two years.

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## Materials and methods

The Division of Laboratory Animal Science has a colony of laboratory rat originally received from the National Centre for Laboratory Animals at the National Institute of Nutrition, Hyderabad. The facility has a policy for conducting necropsy examination on animal carcasses of non-experimental animals resulting from euthanasia or natural death with a view to use the data for health

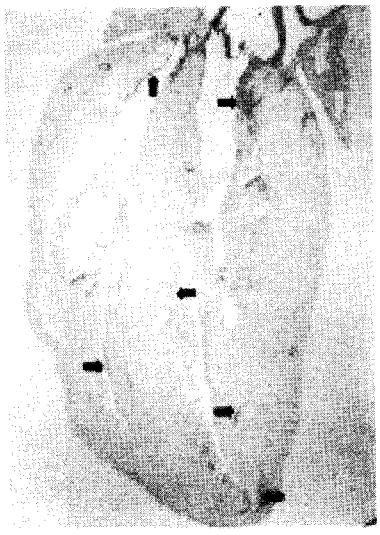

Figure 1: Multifocal distribution of fibrosis seen in ventricles, auricles and tricuspid valves in a rat heart: Van Gieson stain

1. Scientist E, Laboratory for Experimental Pathology, 2. Junior Research Fellow, 3. Senior Technical Assistant, 4. Scientist, Division of Laboratory Animal Science (Corresponding author)

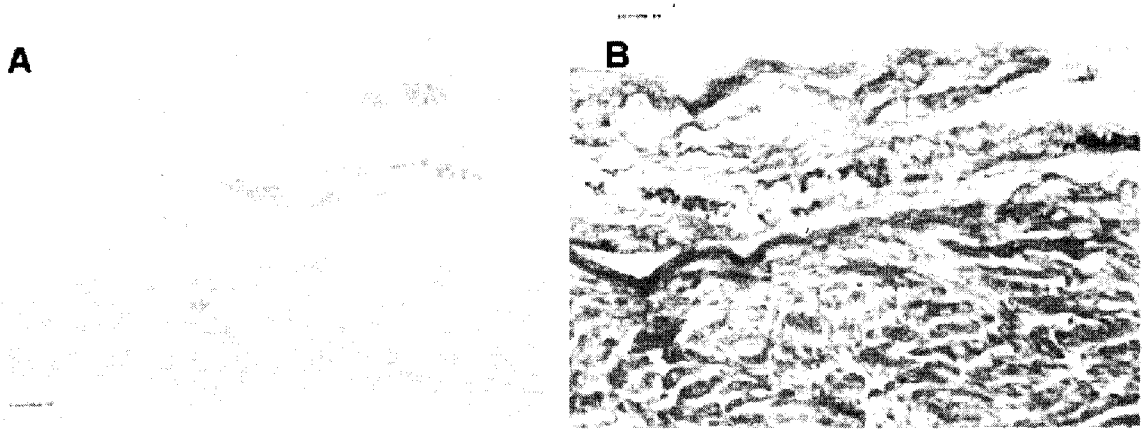


Figure 2: Histopathology of endomyocardial fibrosis demonstrating thick endocardium by routine Haematoxilin and eosin stain (A) Masson's Trichrome stains for collagen (B)

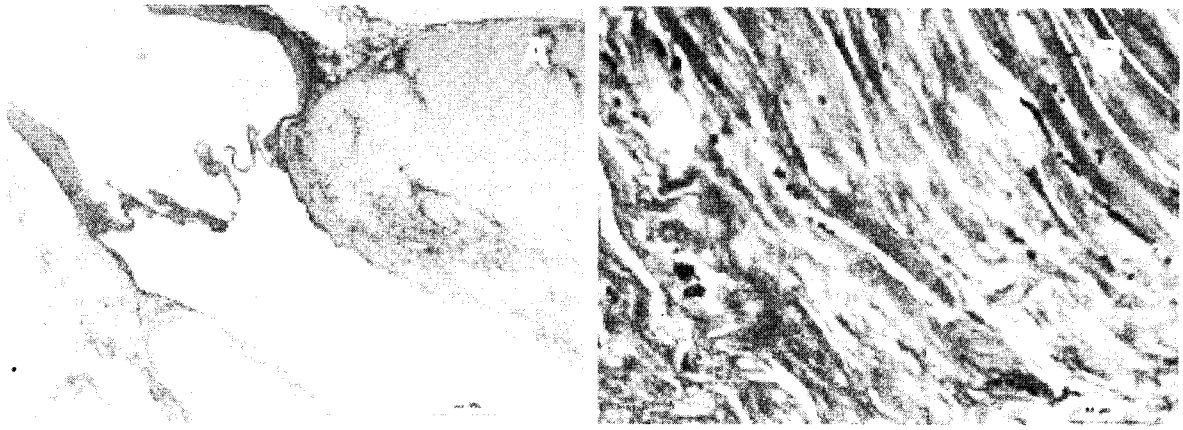

Figure 3: Photomicrograph of heart: myocardial fibrosis demonstrated with Sirius red staining (A) and a healing microinfarct stained with Masson's trichrome stain (B). Note, the red colour (A) and blue colour (B) for distribution of collagen in the diseased area.

monitoring of the animal colony. Endomyocardial lesions reported here were observed in a female rat which was euthanatized due to mammary tumours at 6 months of age. Histology sections of heart were stained with haematoxylin and eosin stains, Masson's trichrome stain, Van Gieson stain and Sirius red (Bancroft and Stevens, 1990).

## Results and Discussion

Endomyocardial fibrosis is essentially a human disease and uncommon among animals (Maxie and Robinson, 2007). However, rat is used as an animal model for the study of induced-EMF as early as 1972 (Lalich *et al.*, 1972) and spontaneous lesions are recorded occasionally (Frith *et al.* 1977) especially in aged animals (Annoni *et al.*, 1998). In the rat, the disease is not often appreciated at necropsy but readily recorded during histopathology. The light microscopic and histopathologic features of the disease in animals are described by Van Vleet and Ferrans (1986). The lesions are either diffuse or patchy in distribution as in this case (Figure 1). The endomyocardium as well as myocardium may undergo variable degree of fibrosis and in the present instance fibrosis was demonstrable by routine haematoxylin and eosin stains (Figure 2), Masson's Trichrome stain (Figure 2) and Sirius red (Figure 3). Infarction is a conjoint feature of EMF and was detected in the present case as well (Figure 3).

Wistar rats are usually susceptible only by the age of 31 months (Vleet and Ferrans, 1986) and the occurrence of EMF in the present instance by the age of 6 months is significant indicating a role for genetic or environmental factors. It is not

sure at this stage if the current observation is only a casual finding. A detailed study of the contribution of genetic factors, dietary habits and environmental influences might be essential for exploring the scope for developing a young rat model for the endemic EMF in young adults in Kerala.

The pathogenesis of EMF is obscure involving multiple factors including dietary and environmental factors. Recently, drugs used for cancer treatment has been shown to induce myocardial fibrosis in rats (Chandran *et al.*, 2009) and dietary modifications can substantially reduce the incidence of experimental EMF in the rat (Seymour *et al.*, 2008) and therefore has renewed interest for having animal models for studying EMF (Varagic *et al.*, 2006) despite differences in human and animal pathology (Naylor *et al.*, 1986). The data presented here suggests that the search for a rat model for human EMF would be profitable in view of the young age of the rat involved and the geo-climatic conditions under which it was reared.

## Conclusion

This short paper describes the histopathology of spontaneous endomyocardial fibrosis in a laboratory rat. The demographic and public health significance of the lesion against the possibility for developing an animal model for human endomyocardial fibrosis are described.

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## References

Annoni G., Luvarà G., Arosio B., Gagliano N., Fiordaliso F., Santambrogio D., Jeremic G., Mircoli L., Latini R., Vergani C., Masson S. (1998). Age-dependent expression of fibrosis-related genes and collagen deposition in the rat myocardium. *Mechanisms of Ageing and Development*, 101(1-2): 57-72.

Bancroft J.D. and Stevens A., (1990). *Theory and practice of histological techniques*, (Churchill Livingstone, Edinburgh), pp: 413.

Bukhman G., Ziegler J., Parry E. (2008) Endomyocardial Fibrosis: still a mystery after 60 Years. *PLoS Negl Trop* 2(2): e97. doi:10.1371/journal.pntd.0000097

Chandran K., Aggarwal D., Migrino R.Q., Joseph J., McAllister D., Konorev E.A., Antholine W.E., Zielonka J., Srinivasan S., Avadhani N.G., Kalyanaraman B. (2009). Doxorubicin inactivates myocardial cytochrome c oxidase in rats: cardioprotection by Mito-Q. *Biophys Journal*, 96(4):1388-1398.

Frith C.H., Farris H.E., Highman B. (1977) Endocardial fibromatous proliferation in a rat. *Laboratory Animal Science*. 27(1):114-117.

Kumar B.P., Shivakumar K., Kartha C.C., Rathinam K. (1996). Magnesium deficiency and cerium promote fibrogenesis in rat heart. *Bulletin of Environmental Contaminant Toxicology*. 57(4):517-24.

Lalich J.J., Allen J.R., Paik W.C. (1972). Myocardial fibrosis and smooth muscle cell hyperplasia in coronary arteries of allylamine-fed rats. *American Journal of Pathology*, 66(2): 225-240.

Maxie M.G., Robinson W.F. (2007), Cardiovascular system. Ed. Maxie M.G., *Jubb. Kennedy. And Palmer's Pathology of Domestic Animals*, 5th ed. Vol 3, pp. 1-105

Naylor D.C., Krinke G., Zak F. (1986). A comparison of endomyocardial disease in the rat with endomyocardial fibrosis in man. *Journal of Comp Pathology*, 96(5): 473-483.

Seymour E.M., Singer A.A., Bennink M.R., Parikh R.V., Kirakosyan A., Kaufman P.B., Bolling S.F. (2008). Chronic intake of a phytochemical-enriched diet reduces cardiac fibrosis and diastolic dysfunction caused by prolonged salt-sensitive hypertension. *Journal of Gerontology A: Biological Sciences and Medical Sciences*. 63(10): 1034-1042.

Van Vleet J.F. and Ferrans V.J. (1986), Myocardial Diseases of Animals *American Journal of Pathology*, 124 (1): 98-178.

Varagic J., Frohlich E.D., Díez J., Susic D., Ahn J., González A. and López B. (2006). Myocardial fibrosis, impaired coronary hemodynamics, and biventricular dysfunction in salt-loaded SHR. American Journal of Physiology: *Heart and Circulation Physiology*, 290(4):H1503-9.

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