ANIMAL MODEL OF HUMAN DISEASE

Endocardial Fibroelastosis

Endocardial Fibroelastosis in Burmese Cats

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PRIMARY ENDOCARDIAL fibroelastosis (EFE) is a congenital anomaly characterized by diffuse fibrous and elastic endocardial thickening in the absence of other important cardiac lesions.[1-3] The left side of the heart is nearly always involved and is usually dilated and hypertrophied. This entity is to be distinguished from diffuse endocardial thickening secondary to one of several congenital cardiovascular malformations (including hypoplastic left ventricle), from viral myocarditis,[4] cardiomyopathy,[5] myocardiosis, myocardial necrosis, and from localized endocardial thickening secondary to a host of endomyocardial injuries.

Biologic Features

Primary EFE is an inherited congenital anomaly of Burmese, and probably of Siamese, cats. It is a common cardiac defect of cats[6,7] and is almost certainly underdiagnosed.[2] The disease is manifest by tachycardia, gallop rhythm, systolic murmur, cardiomegaly, and signs of congestive heart failure, especially dyspnea and often terminal cyanosis. The onset is commonly precipitated by a respiratory infection between 3 weeks and 4 months of age. The course is short; sudden death is not uncommon. Mild forms of the disease with few or no signs allow cats to reach maturity and transmit the defect to offspring. The mode of inheritance appears to be complex and is still under study.

Pathologic lesions are limited to the heart or are secondary to heart failure. Dilation of the left atrium and ventricle is often severe and may cause the wall of the left ventricle to appear thin, despite hypertrophy. The endocardium is thickened throughout the left side and tends to become opaque in older kittens or after formalin fixation. Microscopically, the endocardium is thickened 10–200 μ by a subendothelial layer of delicate collagen and elastic fibers with thick, more organized fibers adjacent to the normal myocardium.

Study of affected Burmese kittens necropsied at various intervals after birth via electron microscopy reveals developmental features. Endocardial edema and dilated lymph vessels present in early stages suggest a vascular derangement such as obstruction of cardiac lymphatics, a condition known to produce

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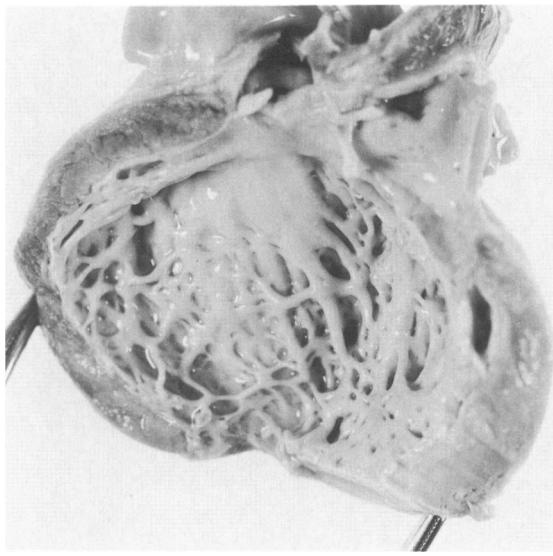

Figure 1—Dilated left ventricle with thickened endocardium from a 1-month-old child with primary EFE.

synthesis. Older fibers become thick and more organized as new fibers are formed near the surface. Purkinje cells become entrapped in the fibroelastic proliferation and tend to undergo atrophy in later stages.

Comparison With Human Disease

The incidence of primary EFE in man is unknown, but it may be much higher than previously thought, since the clinical diagnosis is difficult and milder forms and early stages of the disease may not be recognized even at autopsy.[9] The clinical and pathologic features of EFE in humans[2,3,10] are essentially the same as those described in cats. The etiology and pathogenesis of primary EFE in man are not known. Many reports indicate a familial occurrence, and various modes of inheritance are implicated. Confusion abounds, for many studies fail to differentiate primary EFE from acquired forms and from those forms secondary to various acquired or congenital myocardiopathies.

Usefulness of the Model

The similarities of primary EFE in cats to that in humans is striking. A family of Burmese cats affected with this disease have provided substantial information concerning the etiology and pathogenesis.[1,2] There is much more to learn, especially about the exact time of onset and the mechanisms involved in the earliest changes, the mode of inheritance, and

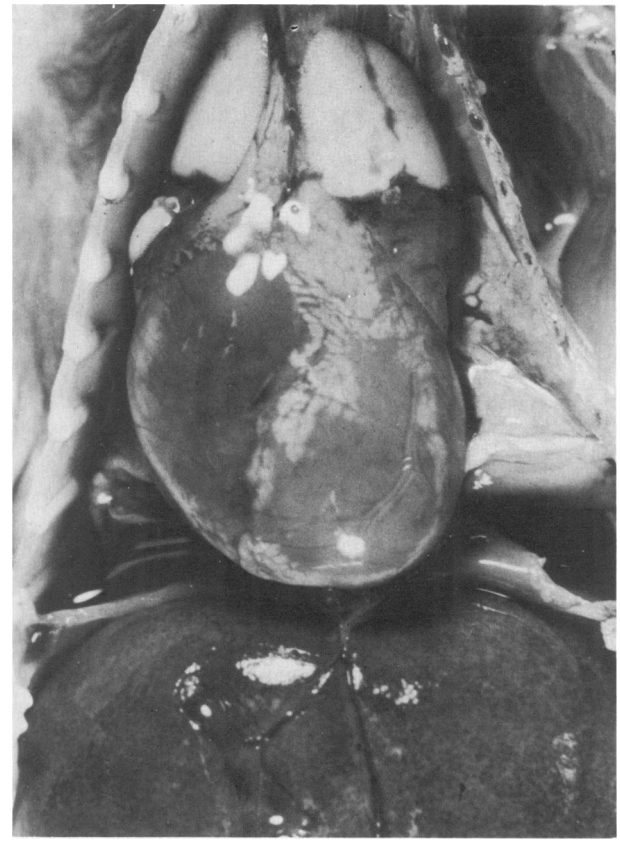

Figure 2—Cardiomegaly and hydrothorax in a Burmese kitten with EFE.

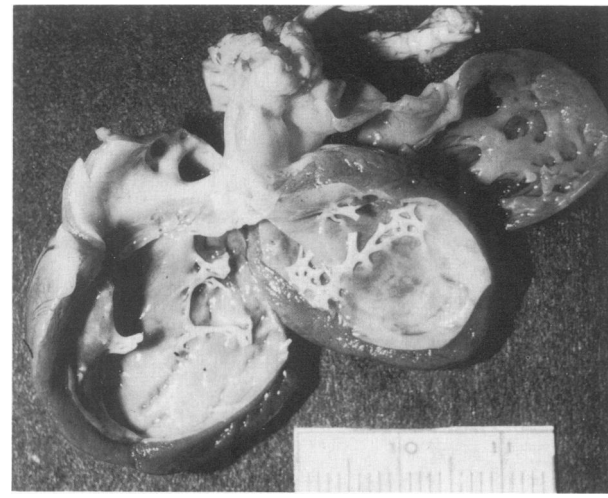

Figure 3—Severely thickened endocardium of the dilated left ventricle from a Siamese cat with primary EFE. Reproduced from Zook[6] with permission of S. Karger AG, Basel.

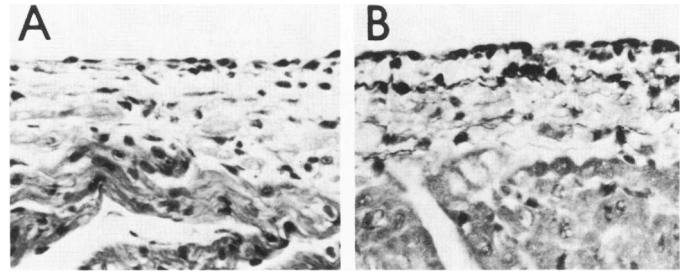

Figure 4—Edematous and cellular thickening of the endocardium from an affected 8-day-old Burmese kitten. **A**, H&E, × 250; **B**, Verhoeff-Van Gieson, × 250)

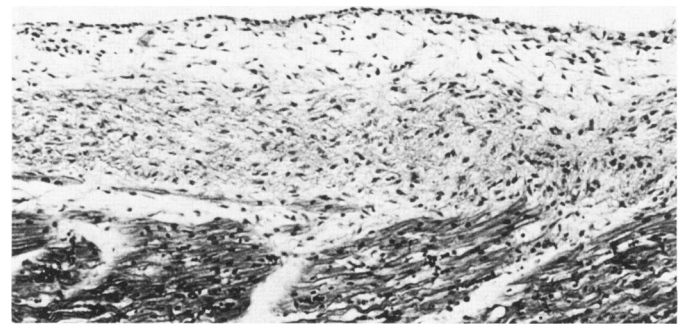

Figure 5—Moderately severe fibrous and elastic thickening of endocardium from a 30-day-old Burmese cat. (H&E, × 150)

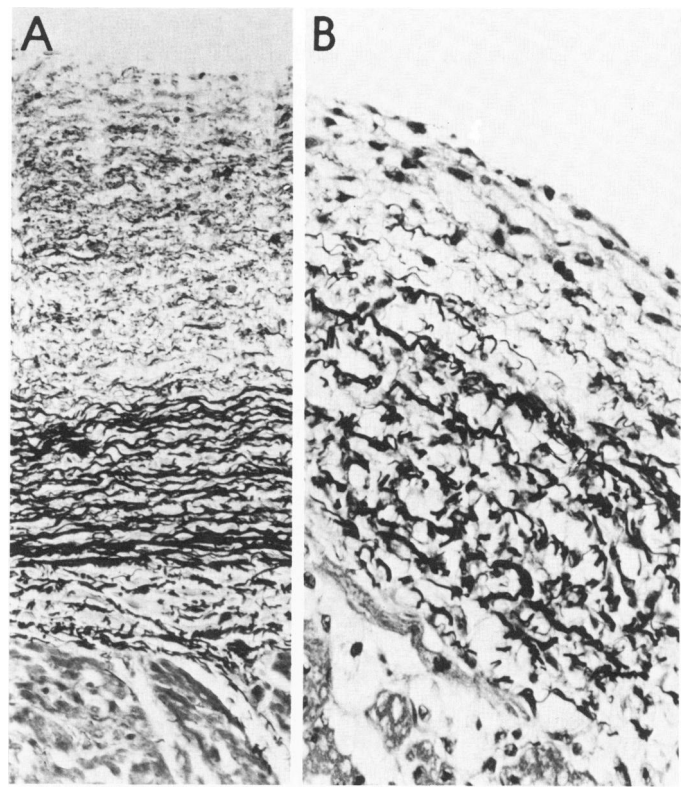

Figure 6—Advanced EFE in a 6-month-old child (**A**) (Verhoeff-Van Gieson, × 250) and a 2-month-old Burmese cat (**B**) (Verhoeff-Van Gieson, × 350). Note the thinner, less organized elastic fibers in the newly forming layer just under the endothelium.

EFE experimentally.[8] The endothelium remains intact and no fibrin nor inflammatory cells are observed. A proliferation of fibroblasts just under the intact endothelium is followed by collagen and elastin fiber whether drugs or other environmental factors can alter the progress of the disease.

Availability

The disease is probably much more common among animals, especially Siamese and Burmese cats, than recognized. Identification of the disease in offspring, acquisition of the parents, and the establishment of breeding colonies are necessary for the disease to be studied effectively. A colony of Burmese cats is being established at this institution, and affected offspring or sperm from affected males may become available in the future.

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