Endomyocardial Neurofibromatosis, Rat*

Peter Bannasch and Doris Mayer

**Synonyms.** Endomyocardial disease, endomyocardial fibromatous proliferation, endomyocardial fibromatosis, endomyocardial fibrosis, subendocardial fibrosis, schwannomatosis, endocardial schwannoma, neurinoma, endocardial tumor.

**Gross Appearance**

With the naked eye no abnormalities are visible in mild cases of the disease. In severe cases, the lesions appear as whitish thickening of the endocardium (Fig. 61) and may even form large tumor masses which bulge into the left ventricle (Boorman et al. 1973). Sometimes endomyocardial neurofibromatosis is combined with hypertrophy of the myocardium.

**Microscopic Features**

As a rule, the lesions are located in the left ventricle, especially in the interventricular septum (Fig. 61). The right ventricle may also be affected, although to a much smaller extent. The leading histologic finding is a thickening of the endocardium in large areas, or even throughout the left ventricle (Boorman et al. 1973; Mayer and Bannasch 1983; Naylor et al. 1986; Landes et al. 1988). Early lesions are characterized by poorly differentiated pale cells with round pleomorphic nuclei, which form a thin layer between the intact endothelium and the elastin bundles of the endocardium. More advanced lesions are predominantly composed of fibroblastic cells with elongated, sometimes undulated nuclei (Fig. 62). The cells are closely associated with collagenic fibers and glycosaminoglycans as demonstrated histochemically by staining with alcian blue. Both cells and fibers are arranged in a highly ordered fashion (Figs. 62, 63), occasionally with a characteristic “herringbone” pattern (Fig. 63). Rarely, mitotic figures are seen. In severe lesions, the thickness may amount to approximately one-half of the ventricular wall or septum. Sometimes a two-layer arrangement is present. Whereas the superficial subendothe-
Endomyocardial Neurofibromatosis, Rat

Fig. 61. Heart, rat with endomyocardial neurofibromatosis in the left ventricle. Note also hypertrophy of the myocardium. (From Mayer and Bannasch 1983) H & E, × 8

The endocardial layer consists of loosely arranged and poorly differentiated pale cells as described above for the early lesions, the deeper layer is made up of densely packed fibroblastic cells and abundant collagen fibers. The lesions may be sharply demarcated from the underlying myocardium but frequently the upper layer of the myocardium is involved in the disease (Fig. 64). In these cases, the myocardium is interwoven with thin bundles of the fibroblastic cells and collagen fibers or split by broader septa which are at places connected with the thickened endocardium. Individual muscle fibers enclosed within the lesions may undergo degenerative changes. In the myocardium adjacent to the lesion small inflammatory infiltrations consisting of lymphocytes and Anitschkow’s cells are rarely seen.

A progression of endomyocardial neurofibromatosis to polyp formations (Fig. 65) and large tumor masses, which protrude into the ventricular lumen or fill large parts of the ventricle, have been observed by a number of authors (Boorman et al. 1973; Ivankovic 1976; Berman et al. 1980; Hoch-Ligeti et al. 1983; Mayer and Bannasch 1983; Naylor et al. 1986). The large tumors resemble well-differentiated fibrosarcomas (Figs. 66, 67). The cellularity of the tumor tissue varies from areas with densely arranged cells to less cellular parts with abundant collagen fibers and occasionally mucoid changes. The nuclei are more pleomorphic in the tumors than in the smaller lesions, sometimes with the Anitschow’s pattern of chromatin. A study of endomyocardial lesions in rats, by Landes et al. (1988), using immunohistochemical methods, utilized lesions in different stages, including ten cases in which the lesions progressed to tumors. These authors found that in the majority of these cases the cells reacted positively to S-100 protein and some were also positive to neuron-specific enolase. In general, S-100 immunoreactivity was weaker in fully developed tumors than in smaller endomyocardial lesions. The presence of S-100 protein has also been observed by immunohistochemical methods in both spontaneous and N-nitrosoethylurea-induced rat endocardial tumors by Turusov and Cabral (1988).

Ultrastructure

Five cases of “subendocardial fibrosis” (Lewis 1980), four cases of early stages of endocardial tumor induced by methylnitrosourea (Holzhause and Schreiber 1977), and two “tumor-like” lesions arising from the endocardium of the rat were studied by electron microscopy (Berman et al. 1980; Naylor et al. 1986) with conflicting results. Berman et al. (1980), who