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Case Report

Connatal Endocardial Myxoma

Case Report and Pathogenesis

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Summary. A case is reported of a Connatal endocardial myxoma in a 5 day old girl. The myxoma was localized at the margin of a high ventricular septal defect. The pathogenesis of endocardial myxomas is discussed taking into account the pertinent literature.

Zusammenfassung. Bericht über ein konnatales Endokardmyxom bei einem 5 Tage alt gewordenen Mädchen. Das Myxom war am Rande eines hochsitzenden Ventrikelseptumdefektes lokalisiert. Die Pathogenese der Endokardmyxome wird unter Berücksichtigung der einschlägigen Literatur diskutiert.

The heterogenous group of cardiac tumors consists of primary and secondary neoplasms, teratomas and choristomas. While tumors of the last two groups are very rare—this is also true for heterotopic branchiogenic tissue in the heart predominantly observed in animals (Kast, 1958)—primary cardiac tumors are of considerable interest in the light of modern diagnostic and therapeutic procedures.

Most of the primary cardiac tumors usually develop from the endocardial layer, while tumors of the pericardium or myocardium are much less frequent. Myxomas represent about 50% of primary cardiac tumors (Bradhurst, 1961; Prichard, 1951; Sybers, 1971).

Pathogenesis of cardiac myxoma has been discussed for many decades. The thrombogenous origin of myxomas first discussed by Thorel (1903) and Husten (1923) was questioned by Huebschmann (1935), Ribbert (1924) and Yater (1931).

The fact, that myxoma represents a true neoplasm appears to be established in the light of recent electron-microscopic and biochemical studies. In special cases of myxoma, however, it may be doubtful, whether it is of thrombogenous or neoplastic origin.

Pathogenesis of myxoma from early embryonic stages of organ development has been discussed by some authors (Heath, 1968; Eck, 1939; v. Meyenburg, 1951), but only few cases of connatal endocardial myxomas have been reported in the past (Eck, 1939; Schink, 1941; Mahaim, 1945). The present study deals with one more case of this type.

Case Report. 5 days old girl. Birth at term. Weight at birth 1810 g. Hydramnion placentae. The infant was immediately admitted to the Pediatric Clinic because multiple malformation was suspected. On the fourth day unexpected cardiac insufficiency. Trisomia 18 could not be excluded since chromosome studies could not be performed. Autopsy was carried out 32 hours after exitus.

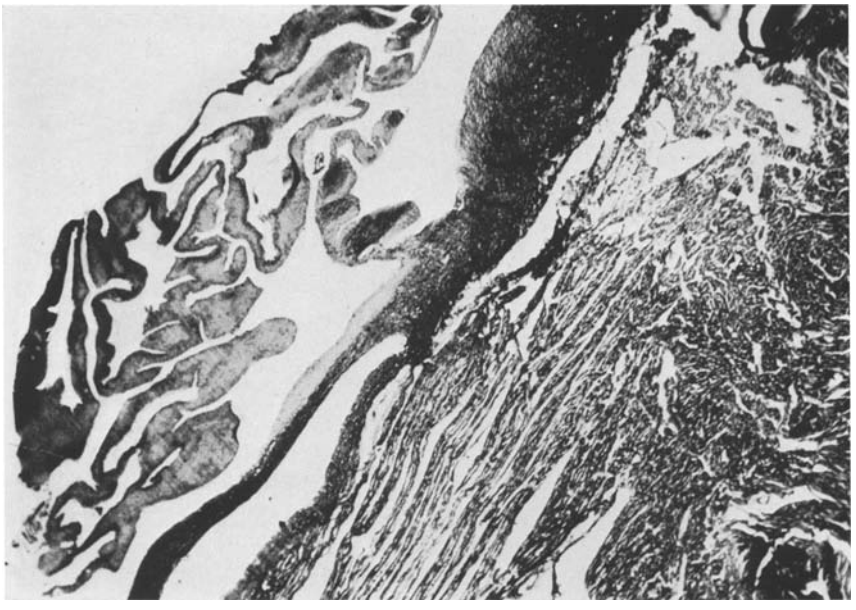

Fig. 1. Cardiac myxoma with L. fibroelastica externa and myocardium. Formalin, paraffin, H.E. Magnif. × 16

Autopsy record no. 388/70: 46 cm size, 1750 g weight. Large defect of ostium primum and secundum with high ventricular septum defect. 5 × 5 × 4 mm papillary endocardial myxoma of the left atrium at the margin of the septum defect. Connatal diaphragmatic hernia on the left side with deplacement of stomach and spleen into the pleural cavity. Atypic Riedel's lobulation of the liver. Bilateral low-lying of the ears, bilateral pes varus.

Microscopic Investigation. The slides were stained with hematoxylin-eosin, Gomori's reticulin stain, periodic acid Schiff, mucicarmin, alcian blue, Goldner trichrome, Prussian blue, toluidene blue, elastica-van Gieson, phosphotungstic acid-hematoxylin.

The tumor originates from the margin of the septum defect with a broad basis. The papillae are up to 4 mm long and 200–400 μ broad (Fig. 1). The surface is covered by endothelium showing a continuous transition into the endothelium of the endocardial layer at the basis. The endocardium at the basis measures up to 40 μ, the L. fibroelastica externa 1.2 mm. The remaining endocardium appears as an inconspicious flat layer separated from the myocardium by elastic and collagenous subendocardial tissue. The basis of the papillary tumor contains a considerable amount of collagenous fibrils which in part radiate into the myocardium; but no vessels, smooth muscle fibrils or elastic fibers. The mesenchym of the tumor consists of loose mucoid ground substance with some collagenous fibrils. The nuclei of the stroma cells are of ovoid, sometimes of stellate shape (Fig. 2). Only few fragments of argyrophilic fibers are observed. Focally the stroma stains faintly positive with alcian blue 8 GS and toluidene blue and strongly positive with periodic acid Schiff, especially around the collagen fibrils.

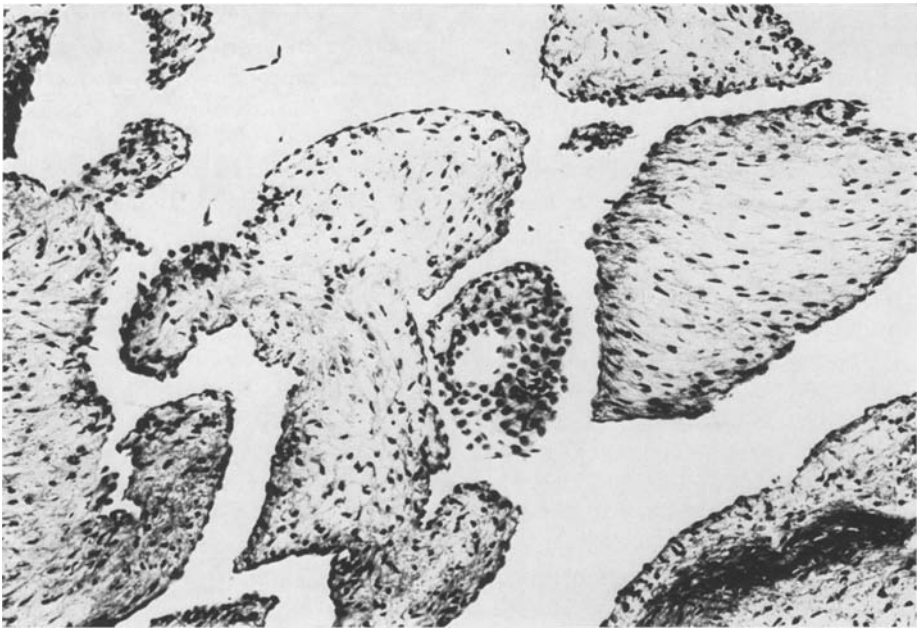

Fig. 2. Cardiac myxoma, higher magnification. Formalin, paraffin, periodic acid Schiff. Magnif. × 150

No staining with mucicarmin, no hemosiderosis. No fibrin demonstrable by staining with phosphotungstic acid-hematoxylin.

Diagnosis: Connatal papillary endocardial myxoma.

Discussion

Endocardial myxomas are rare tumors. According to the reviews given by Straus and Merliss (1945) and Heath (1968) they represent 0.0017% to 0.025% of unselected autopsy cases. In the past most cases of endocardial myxomas were obtained from autopsy material (Mahaim, 1945) while in recent time clinical reports prevail. In 1952 Goldberg was the first who made the diagnosis of endocardial myxoma intra vitam, and in the last years several patients underwent successful surgical treatment (lit. see Schmidt-Habelmann, 1965).

No consistent data exist in regard to *age and sex distribution*. Some authors state that myxoma is more frequent in females than in males (Bradhurst, 1961; Fine, 1968a). An evaluation of numerous case reports and reviews gives evidence that endocardial myxomas occur 2 to 3 times more frequent in females and predominantly in patients from 30 to 60 years of age. Cases of myxoma in children have been reported very rarely.

The *clinical picture* shows considerable variations and depends mainly on the *localization and size of the tumor*. More than 75% of all endocardial myxomas are localized in the left atrium, especially in the region of the fossa ovalis. Symptoms are cardiac murmur and signs of mitral stenosis. Differential diagnosis

to subacute endocarditis can be difficult because of slight fever and arrhythmia present in some cases (Bradhurst, 1961). Frequently endocardial myxoma of the left ventricle is followed by recurring arterial embolism into the organs of systemic circulation. If the myxoma is localized in the right heart, the clinical picture may be confused with tricuspidal stenosis, pulmonary thromboembolism or constrictive pericarditis. Often it is characterized by cyanosis and pulmonary hypertension (Bradhurst, 1961; Fine, 1968a; Heath, 1964; Prichard, 1951; Schmidt-Habelmann, 1965; Sybers, 1971). Rarely myxoma is localized on the cardiac valves (Eck, 1939; Kaiser, 1962). Differentiation from excrescences of Lambl may be difficult especially since the latter may also occur in the atrial endocardium (Sinapius, 1955).

Two main theories exist concerning the *pathogenesis* of endocardial myxoma:

In 1903 Thorel reviewed the pertinent literature. In contrast to Marchand (1894) and Ribbert (1924) he came to the conclusion that endocardial myxoma must in all cases be considered as organized endocardial thrombi having undergone degenerative changes. This view was supported by Husten (1923) with regard to results obtained in a review of several cases. Recently the thrombogenic origin of endocardial myxoma has again been stressed by Zollinger (1969).

Ribbert (1924) denied the theory that all myxomas derive from thrombi of the cardiac wall. He believed that at least some cases were proven true neoplasms. In Ribbert's opinion substantial evidence for this view would result from the localization of cardiac myxomas, especially within the left atrium, while most atrial thrombi are in the auricular appendage, from the macroscopic appearence of the usually pedunculated tumors and from the lack of evidence for the organization of thrombi. According to Ribbert the structures resembling thrombi are caused by hemorrhages into the myxoma. The different microscopic picture of the endocardial myxoma is expressed by the variety of synonyms: myxoma, myxofibroma, elastomyxoma, fibroangiomyxoma, hemangioelastomyxoma, fibroelastomyxoma etc. The neoplastic nature of some cases of endocardial myxoma has been confirmed by tumor emboli into the pulmonary vessels (Heath, 1964) and by case reports of malignant endocardial myxoma (Huebschmann, 1935; Rutkai, 1963).

Two cases of endocardial myxoma in newborn infants were described by Eck (1939) and Schink (1941) and interpreted in favor of the theory that endocardial myxoma might arise from visceral mesodermal tissue and should be classified as hamartomas (see also Marchand, 1894; Lubarsch, 1895; Borst, 1936).

Recent biochemical (Dubach and Gsell, 1964), histochemical and electron-microscopic results leave no doubt that endocardial myxomas may be of true neoplastic nature. The quantitative biochemical investigation of myxoma tissue resulted in absolutely different activities compared to normal myocardial tissue (Dubach and Gsell, 1964). A comparison appears to be permitted since apart from the endothelial layer endocardial myxoma corresponds to the structures of the L. fibroelastica externa which, like the myocardium, arises from the outer layer of the fetal myoepicardial coat (Becker, 1964; Lannigan, 1966).

In electron-microscopic studies the ultrastructure of myxoma cells is rather a combination of that seen in the surface layer cells and the mesenchymal stroma cells, than that of a special type of endocardial cell. These cells, sometimes called

"lepidic cells", perhaps represent cells of mesenchymal origin with secretory function (Fine, 1968b).

The fact that myxoma predominantly originates from the endocardium of the left atrium, supports the theory that myxomas may belong to the group of hamartomas since the thickest layer of endocardium is found at the same site (Remmele and Haag, 1970; Haack, 1971).

The similar microscopic structure of the endocardial tumor in the present case and of the fetal cardiac anlage (Fig. 2) suggests that cardiac myxoma may develop during organic development. The aperture between the endocardium and the myoepicardial coat which is composed of loose gelatinous substance ("gelatinous reticulum", Starck, 1965) undergoes cellular organization from the side of endocardium. The common ostium atrioventriculare is subdivided by septa originating from the endo- and myocardium. Finally, the foramen interventriculare is closed after the embryo measures 17–22 mm (Goerttler, 1968).

However, the proliferative potential may be preserved from the time of embryonic development to adult stage. This may be concluded from secondary closure of defects of the ventricular septum (Bloomfield, 1961; Goerttler, 1968). The present case may be regarded as an attempt of the endocardium towards a healing of the ventricular septum defect, since the myxoma was localized at the margin of the defect. The same interpretation may be true for the frequent occurrence of endocardial myxomas in the region of the fossa ovalis. The partial defects of the atrial septum (ostium secundum defects) are closed post partum only by proliferation of the endothelium of the septum primum and secundum. Consequently, endocardial intercrescences of this region may be found frequently in children. The false chordae tendineae which can be found in the fossa ovalis of the adult may be explained in the same way (Franck, 1970).

The interpretation of endocardial myxomas as a result of disturbed embryonic development, applies to only a few cases. However, it may be true that proliferation of endocardium is responsible for the development of endocardial myxomas in later age. The differentiation between a parietal endocardial thrombus and a true neoplastic myxoma may be difficult in one case or another. Differential diagnosis may be facilitated by the criteria described by Fine (1968a).

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