Case Reports

A Case of Constrictive Endocardial Sclerosis Accompanied with Congenital Lutembacher's Syndrome

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LUTEMBACHER'S syndrome was first described by Martineau in 1865, and detailed report was made by Lutembacher in 1916. The syndrome, a combination of mitral stenosis and atrial septal defect, was at first considered as congenital origin. However, in recent years most of the mitral stenosis in such cases have been considered as acquired origin.

Congenital mitral stenosis is a type of the hypoplastic left heart syndrome, and one of the relatively uncommon type of congenital malformation of the heart. A combination of congenital mitral stenosis with atrial septal defect is a more uncommon condition.

Endocardial sclerosis or fibroelastosis was assumed to be one of the relatively common causes of cardiac death in infancy,^{1), 2)} and many cases have been reported in the recent years. Though this disease was recognized as a well-described entity,³⁾ extensive morphological varieties corresponding to various nomenclatures such as fetal endocarditis or endomyocarditis,⁴⁾ primary or prenatal endocardial fibroelastosis,^{3), 5), 8), 12) - 24)} endocardial dysplasia⁶⁾ and endocardial sclerosis,^{1), 7), 39)} are present and the cause and the nature of this disease are still obscure. It is believed that an accumulation of the experiences of many cases will elucidate these problems. The present report represents the authors' experience on a case showing Lutembacher's syndrome associated with pathologically characteristic constrictive endocardial sclerosis.

CASE REPORT

A 2½-month-old boy was admitted to the Tokyo University Hospital with the chief complaint of hematuria. His family history was non-contributory. The delivery was uncomplicated and the patient weighed 3.2Kg. at the birth. The mother had some episode of fever and abdominal pain during the second month of pregnancy. After the birth cyanosis was noticed while crying. At 2 months of age a cardiac murmur was noticed. The x-ray examination of the chest and

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ECG examination revealed a possibility of common ventricle. Hematopyuria became better after one week admission and he was discharged.

When he reached 4-month-old, he was admitted again to the Tokyo University Hospital with the chief complaints of slight edema and dyspnea of a few days' duration. Physical examination revealed a malnourished baby weighing 5.3 Kg., and a feeble pulse, tachycardia, cyanosis, dyspnea and slight edema were observed. Moist râles were heard over the entire lung field and the systolic cardiac murmur of grade 3 was heard at the left lower sternal border. The chest x-ray film revealed an enlarged cardiac silhouette to the both sides, protruded pulmonary conus and pulmonary congestion (Fig. 1).

Fig. 1. X-ray finding of Lutembacher's syndrome.

Electrocardiogram showed the finding of right ventricular hypertrophy with a positive T-wave in V_1 , a tall R_{V_1} and deep S_{V_6} . The QRS complex of all chest leads showed RS-pattern and the diagnosis of common ventricle was suspected. A tall P waves were found in leads I, II, III and V_1 which indicate the presence of right atrial enlargement (Fig. 2). Peripheral blood picture showed polycythemia, 630×10^4 of RBC and 22.4 Gm./100 ml. of Hgb. and leucocytosis of 18,800 with lymphocytosis.

The patient died 5 hours after the admission despite an extensive treatment with cardiotonica and oxygen administration.

Gross autopsy findings:

The body was moderately well developed, fairly well nourished and 7 Kg. in body weight. The abdomen was somewhat bloating and there was slight pitting edema on the lower extremities. The peritoneal and pleural cavities on both sides contained 20 ml. of clear, amber-colored fluid, and the pericardial sac contained 10 ml. of the similar fluid. A markedly enlarged liver was observed 4 finger breadth below the costal margin in the median line.

The heart, which weighed 135 Gm. (expected weight; 40.5 Gm.), was enormously enlarged showing a globular form. Both of the right ventricle, of which the cardiac apex was composed, and the right atrium were strikingly dilated and

Fig. 2. ECG finding of Lutembacher's syndrome.

Fig. 3. (a) The right side of the heart. Marked dilatation and hypertrophy of the right ventricle and atrium. Note the patchy endocardial thickenings. The arrow mark indicates the patent foramen ovale.

(b) The left side of the heart. Marked endocardial thickening in the left ventricle and moderate thickening in the atrium. Slightly thickened leaflets of the mitral valve and reduced mitral ostium.

(c) The contracted cavity of the left ventricle. The fibrous endocardium is measured by 1 to 3 mm. in thickness. Almost normal cusps of the aortic valve. This illustration is enlarged to a greater extent than a and b.

hypertrophied (Fig. 3, a and Table I). The left ventricle, on the contrary, was as small as thumb-tip sized in its cavity (Fig. 3, b and c). The left atrium was also as small as almost a half of the right atrium. The striking difference in

Table I
Heart Measurements (after fixation)

Volume of each cavities (ml.):		
Left ventricle	4	Left atrium 7
Right ventricle	13	Right atrium 13
Wall thickness (mm.):		
Left ventricle;		Left atrium 2.0
Apex.....	6.3	
Median	7.0	
Outflow tract.....	7.0	
Right ventricle;		Right atrium 2.6
Apex.....	4.4	
Median	5.3	
Pulm. conus	9.4	
Valvular thickness (mm.):		
Mitral	0.5	Aortic 0.4
Tricuspid	0.4	Pulmonary 0.3
Circumference of orifices (mm.):		
Mitral	35	Aortic 35
Tricuspid	63	Pulmonary 34

size between the both ventricles made the left appear as an appendage of the right. The mural endocardium covering the left ventricle and atrium, showed diffuse, gray-whitish discoloration and a marked thickening. It was especially marked in the contracted left ventricle measuring 1 to 3mm. thick and had trabeculated, irregular surface being ill-defined with the underlying myocardium which was not so hypertrophic (Fig. 3, c). The endocardium of the left atrium showed a moderate degree of diffuse thickening with relatively smooth surface. On the right side, the endocardial thickening was of much lesser extent and patchy in appearance. The patchy thickenings were disseminated on the moderator band, the papillary muscles and the edge of foramen ovale as well as the trabeculated posterior surface of the right atrium (Fig. 3, a). Two leaflets of the mitral valve and their chordae tendinae were also involved and appeared slightly thickened and they were in somewhat stenotic condition. The mitral ostium was significantly narrower than the tricuspid one which was markedly dilated. The cusps of the aortic valve were almost normal in their size and thickness as well as that of pulmonary valve. The foramen ovale was patent about 4mm. in longer diameter, with an efficient valve-like fold of endocardium. The ductus arteriosus was functionally closed already. No other abnormalities were observed in the heart. Some data from the cardiac measurements were summarized in Table I.

Moderate to severe congestion was observed in the lungs, liver, spleen and kidneys. The thyroid and adrenal glands did not show any gross abnormality as well as other endocrine organs.

Microscopic findings:

The thickened mural endocardium in the left ventricle was composed

chiefly of a marked hyperplasia of interlacing bundles of collagen connective tissue (Fig. 4, a). A number of nodular, delicate myxomatous structures having the similar feature of embryonic endocardium, were disseminated among

Fig. 4. (a) Marked thickening of the mural endocardium in the left ventricle. Nodular myxomatous tissue is observed in the left side of the illustration. Irregularly arranged collagen tissue is noted. $40\times$. Weigert's elastic tissue stain and counter-stained with van Gieson's connective tissue stain.

(b) The endocardial fibrous tissue extends into the underlying myocardium. In the deep layer of the endocardium, dense collagen fibers were interlaced with increased elastic fibers. Note prominent dilated sinusoids in the tongue-like projections of the fibrous tissue. $100\times$. Stained by the same method as (a).

somewhat irregularly arranged collagen tissue layer, in which slightly increased delicate elastic fibers and pink-red stained amorphous materials by PAS method were contained. The connective tissue extended in many areas as finger-like projections between the underlying myocardial fibers, and each of them contained many prominent dilated sinusoids assumed to be the Thebesian vessels (Fig. 4, b). The myocardium of the left ventricle showed practically no abnormality except moderate interstitial edema. Slightly thickened mitral valves were composed of almost similar changes as in the mural endocardium but with lesser degree than the latter. Vascularization, fibrosis and cellular infiltration, which might indicate an inflammatory sign, were not encountered throughout any tissue specimens. The patchy endocardial thickening in the right side of the heart was composed of fibroelastosis in which increased collagen and elastic fibers took a regular arrangement being parallel with the lumen. In the myocardium of the right ventricle there were prominent pericellular edema and fibrosis between the moderately hypertrophied muscle fibers. The vascular system in the heart was generally normal except for the Thebesian vessels.

Microscopic examination of the lungs revealed medial hypertrophy and intimal fibrosis in the small arteries, capillary engorgement and intraalveolar collections of many heart failure cells. The liver exhibited a marked central congestion associated with moderate fatty deposition in the parenchymal cells. Prominent venous engorgement was also observed in the spleen and kidneys.

DISCUSSION

Congenital mitral stenosis is relatively rare condition. Ferencz⁴⁴⁾ investigated the reported cases from the literature and decided that the cases considered as truly congenital origin were only 34 cases, and he added his own 9 cases in 1954. A few reports followed Ferencz.^{45), 46)} The association of atrial septal defect with the congenital mitral stenosis was found in only 8 cases among the reported 43 cases of Ferencz, and main complication of mitral stenosis was the anomalies of aorta, aortic valve and patent ducts arteriosus. In Japan, the authors reported 2 cases of congenital Lutembacher's syndrome previously.⁴⁷⁾

In the most cases of Lutembacher's syndrome the nature of mitral stenosis has been considered to be rheumatic in origin. And true congenital Lutembacher's syndrome is considered as a rare condition. Congenital mitral stenosis is one of the types of hypoplastic left heart syndrome, and the underdevelopment of left heart is the characteristic finding. Noonan and Nadas⁴⁸⁾ reported 101 cases of hypoplastic left heart syndrome over 9 years, in which 5 uncomplicated cases of mitral stenosis were included. They also reported that 65% of the cases died within 35 days and 82% within 3 months of age.

In the pathological view point, this case had several characteristic features as follows:

(1) The prominent constrictive nature of the endocardium in the left ventricle diminishes expansibility and contractility^{8), 9)} of its wall and this, cooperating with some thickening of the mitral valves, can show hemodynamic changes identical to those seen in acquired mitral stenosis. The vascular changes in the lungs, marked dilatation, hypertrophy and fibrosis of the right ventricle and patent foramen ovale may be secondary phenomena resembled with those of mitral stenosis. Absence of a dilated left atrium is due to the involvement of fibroelastic process upon it.

(2) The coexistence of nodular myxomatous tissue and fibrosis in the thickened endocardium suggests that the myxomatous tissue,⁷⁾ resembled to the embryonic endocardium or a sort of degenerating fibrotic tissue,¹⁵⁾ is rather fresh process and the fibroelastosis is a successive sequelae of the former. If this assumption is correct, the previously asserted explanation based on electron-microscopic findings,¹⁰⁾ on the pathogenesis of fibroelastosis which started with superficial deposition of fibrin, can not be applied to this case.

(3) Absence of a marked increase in the elastic fibers and delicate or fine quality of them were encountered in the left ventricle. This evidence may show whether the time interval from establishment of the endocardial fibrosis was too short, or the contracted ventricle could not

afford any dilatation or distension of the wall sufficient to stimulate new formation of elastic tissues.¹¹⁾ Since the prominently dilated right ventricle and atrium had a regular fibroelastosis with the thicker elastic fibers, it is supposed that constrictive endocardial sclerosis with no elastic increase in the left ventricle is not essentially different from the fibroelastosis of dilated type, while the endocardial fibroelastosis can also occur as the secondary change resulting from the primary myocardial disease^{12), 16), 21)} and the constrictive endocardial sclerosis is always assumed as the primary endocardial involvement, and may be the initial changes of the latter.

(4) Practically normal myocardial fibers were observed in the left ventricle. This indicates that the endocardial lesion in this case might be primary. Descriptions of the coexistence of the endocardial fibroelastosis and myocardial degeneration have been commonly found in the adult type of fibroelastosis.^{13), 14)} This evidence indicates that the long-persisting circulatory disturbance in the subendocardial muscle fibers, resulting from the stenosing or obstructing Thebesian vessels due to secondary endocardial involvement, were responsible for that of the primary myocardial involvements^{12), 16), 21)} and in some cases endocardial fibroelastosis was accompanied with the primary myocardial disease.

(5) Many previously reported cases of fibroelastosis had closed foramen ovale,¹⁸⁾⁻²⁰⁾ and Johnson¹⁹⁾ inserted the premature fibrous tissue proliferation at the foramen ovale as a cause of fibroelastosis. This was one of supports for anoxic theory as the pathogenesis of fibroelastosis, having identical effect with the case of aberrant left coronary artery.²⁰⁾ The patent foramen ovale in this case, though it is the secondary or compensatory process, reveals that the closing of that was not always essential for the establishment of the fibroelastosis.

(6) Coexistence of the fibroelastosis and many other malformations such as valvular atresia^{4), 22)} or stenosis,^{22), 25)} aortic coarctation,²⁴⁾ patent ductus arteriosus^{22), 24), 25)} and dextrocardia²⁶⁾ makes the fibroelastosis assumed as a part of congenital developmental anomaly as well as the secondary sequelae from the various other anomalies. Anderson and Kelly¹⁷⁾ mentioned that the fibroelastosis was commonly conspicuous in congenitally malformed hearts and suggested the pathogenesis of the fibroelastosis as functional or secondary due to partial anoxia resulting from the malformation. This case had also the patent foramen ovale and slight degree of mitral stenosis as associated anomalies. Excluding the former, however, the thickening of the leaflets of mitral valve, for its minimal degree, is not assumed as any cause of the endocardial sclerosis in this case. Moreover, the similar histologic features between the valvular leaflets and the parietal endocardium suggest that the same process involved both of them but in lesser degree in the valves.

In the previous reports, the endocardial involvements affected chiefly the left side of the heart particularly the ventricle,^{1), 3), 4), 8), 12), 13), 16), 22), 27)-32)} and when the lesion is sufficiently severe, it extended into the valves^{3), 15), 24), 27), 29), 31), 32)} near the lesion. However, the malignant carcinoid syndrome,³³⁾ pulmonary atresia²⁸⁾ and tricuspid stenosis,^{23), 25)} though they were rare, were mentioned as causes of fibrosis or fibroelastosis in the right side. They affected mainly both valvular and mural endocardium, but rarely affected isolatedly the mural one.^{24), 34)}

As to the pathogenesis of this disease, earlier opinions favoring inflammatory factors^{4), 35)-38)} were abandoned since the critical reviews of Gross,^{29), 39)} Cosgrove and Kaump⁷⁾ on the developmental basis of the primary endocardial sclerosis. However, a few cases⁴³⁾ associated with generalized involvement suggesting other causes excluding congenital factor, still remained to be explained. The hereditary factors^{40), 41)} or congenital metabolic disturbance in the myocardium^{6), 12), 42)} were proved in some cases of this disease. The authors pay attention to the evidence that the dilated type of them includes some cases of secondary endocardial fibroelastosis due to the primary myocardial lesion. At the present stage, the pathogenesis of this disease is assumed chiefly as congenital but cannot be defined as a single cause.^{1), 2)}

As the conclusion, this case was considered as a contracted type of the endocardial sclerosis in the congenital and primary nature, and the most appropriate term for this case must be the "constrictive endocardial sclerosis" by Burchell.

SUMMARY

A 4-month-old boy with congenital Lutembacher's syndrome was reported. In the underdeveloped left ventricle, characteristic constrictive endocardial sclerosis, which contained very few elastic fibers and showed nodular myxomatous feature with fibrosis, was found. The characteristic endocardial involvement may be called as "constrictive endocardial sclerosis."

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