Case Reports

Two Cases of Marfan's Syndrome Associated Respectively with Subacute Bacterial Endocarditis and the Wolff-Parkinson-White Syndrome

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SUMMARY

Marfan's syndrome itself is not a very uncommon disease. However, when it is associated with subacute bacterial endocarditis or the W. P. W. syndrome, its scarcity seems to be worthy of notice. As far as we know, there have been only a few cases of Marfan's syndrome with subacute bacterial endocarditis and none with the W.P.W. syndrome.

Two cases of Marfan's syndrome respectively associated with subacute bacterial endocarditis and the W.P.W. syndrome were presented.

Congenital septal defects were demonstrated in one of these cases. The combination of Marfan's syndrome with congenital septal defect or the W.P.W. syndrome seems to be coincidental to each other.

Additional Indexing Words:

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Phonocardiograms

SINCE Marfan's original description in 1896, many cases with the syndrome have been reported to date.¹⁾ It is rather strange, however, that few cases of the syndrome associated with subacute bacterial endocarditis have been reported in spite of the vulnerability of congenital heart defect or acquired deformed valves to bacterial infection. On the other hand, we do not know any report on Marfan's syndrome associated with the Wolff-Parkinson-White (W.P.W.) syndrome.

Two cases of Marfan's syndrome with such a rare complication are presented.

CASE REPORTS

Case 1. A 17-year-old high school boy was admitted to the Tokyo Medical

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and Dental University Hospital in June, 1965, complaining of dyspnea, continued fever and weakness of the left lower extremity. The family history was noncontributory except for myopia in his siblings and mother. A few months after birth, the funnel chest and long fingers were noticed. He had been healthy until the age of 14, when he was taken ill with pneumonia, and then he was told that he had a murmur. Thereafter, there were episodes of fever lasting for about a month, 3 times a year, and kyphoscoliosis was noted. On March 17, 1965, he had a remittent fever of 37°C in the morning and 39°C in the evening, without receiving any treatment for about one month.

In April, 1965, a few reddish painful erythema like sudamina appeared on the sole and extensor of the left forearm. A physician administered oral antibiotics for 3 days and his fever decreased in about one week. On June 4, he suddenly had a headache, and 3 days later he felt a mild hemiparesis of the left leg and difficulty in walking. Since 2 days before admission, fever increased to 40°C and he complained of dyspnea.

He had no history of recent dental treatment.

Physical findings :

He appeared extremely emaciated and pale. The body height was 165 cm. and the weight 40 Kg. There was no petechia, Osler's node or Janeway's lesion. There was a marked kyphoscoliosis due to the thoracic spine curving near the 5th-7th thoracic vertebrae, backward and to the right. Cardiac impulse was visible in the 6th intercostal space on the anterior axillary line. A grade 5/6 rough systolic murmur was audible over the apex. There was also a grade 3/6 systolic murmur in the pulmonic and aortic area with accentuation of A₂. Lungs were clear. Liver, spleen and kidney were not palpable. Neurological abnormalities were absent except for weak Achilles reflexes.

Since the heart on chest X-ray film was extremely displaced to the left, the cardiac contour could not be delineated accurately (Fig. 1). However, there were convexity, elongation and bulging of the left and upper cardiac contour, suggesting

Fig. 1. Postero-anterior chest X-ray film showing marked scoliosis and cardiomegaly.

Fig. 2. Electrocardiogram. A mean QRS axis of $+120$ and presence of S in the left precordial leads are suggestive of right ventricular hypertrophy. There are diphasic P waves with peaked positive component in the lead V_1 - V_2 , which show atrial overloading especially of the right atrium.

left ventricular enlargement. Abnormalities were absent in the lungs.

Electrocardiogram showed sinus tachycardia with a rate of 136/min., and atrial overloading plus a right ventricular hypertrophy (Fig. 2). Urinalysis showed a large quantity of albumin with 8 to 12 red blood cells and 10 to 20 white blood cells per high power field. Serologic studies revealed a strong positive CRP, a weak positive RA, but ASLO of 166 Todd units. The urine culture was negative but 2 blood cultures produced streptococcus viridans sensitive to penicillin, tetracycline and chloramphenicol.

On June 11, 1965, treatment was instituted with intramuscular administration of 1.2 million units of penicillin and 1 Gm. of kanamycin daily. He was also digitalized with a maintenance dose of 0.1 mg. The dose of penicillin was increased to 3.6 million units and that of kanamycin also to 2 Gm. daily after 3 days. On the 8th day after admission, 10 million units of penicillin were administered intravenously, to which was added 0.5 Gm. of probenecid every 6 hours orally, with no improvement. He had a chest pain and orthopnea on June 21 when the levels of lactic dehydrogenase and α -hydroxybutyric dehydrogenase were 982, 693 units, respectively, despite a normal level of glutamic oxaloacetic transaminase. On June 24 digitoxin was increased to 0.2 mg., but again decreased to 0.1 mg. and on June 26 when he complained of left chest pain seemingly due to the infarction of the lung intravenous administration of penicillin was replaced by the intramuscular administration of 5.4 million units of penicillin and 2 Gm. of erythromycin orally. On June 30 dyspnea increased. When edema was observed in the legs on July 3, 20 mg. of furosemide was given intramuscularly. On the following day orthopnea devel-

oped, and on July 7 the blood pressure dropped to 94/50 mm.Hg. On July 8 he died of cardiac insufficiency.

Autopsy findings :

There was evidence of Marfan's syndrome consisting of arachnodactyly of fingers and toes, kyphoscoliosis convex to the right near the thoracic vertebrae, marked funnel chest, slender and long bone of the extremities, poor muscular development and few subcutaneous fat tissue.

The weight of heart was 640 Gm. There were arrested endocarditis lenta with slight ulceration and irregular fibrous thickening of the mitral valve which suggested mitral incompetence. The soy and red bean-sized aneurysms of the posterior leaflet with two small perforations were observed. There were marked fibrous thickening of the endocardium and soy bean-sized pedunculated verrucae of the left atrium adjacent to the mitral posterior leaflet (Fig. 3). Marked dilatative hypertrophy of both ventricles and marked dilatation of the atria of the heart were

Fig. 3. Dilatation of left atrium and changes of mitral valve.

There are slight ulceration and irregular fibrous thickening of the mitral valve. Soy and red bean-sized aneurysm of the posterior leaflet with two small perforation is observed. There are marked fibrous thickening of the endocardium and a soy bean-sized pedunculated verrucae of the left atrium adjacent to the mitral posterior leaflet. These findings show the presence of mitral insufficiency and subacute endocarditis.

Fig. 4. The surface of mitral valve is covered with degenerative products of valve membrane containing neutrocytes and fibrin. In the deeper tissue there are increased histiocytes and granulation which consists of proliferation of fibroblasts. Hematoxylin and eosin, $\times 100$.

present. Slight fibrous pericarditis was present. Other findings showed slight congestion of the left lung (250 Gm.) and diffuse pneumonia in the stage of gray hepatisation of the right lung (950 Gm.), moderate congestion of the liver and kidney and swelling of the spleen.

Microscopically, the ulcers were covered with fibrin containing bacterial clusters and a few leukocytes. There was subendocardial exudation of fibrin in other parts with slight proliferation of mononuclear cells and perivascular increase of plasma cells (Fig. 4). A few foci of myocardial necrosis were replaced by a fresh granulation tissue. There were no Aschoff's bodies. *Streptococcus viridans* was cultured from the heart blood.

Case 2. A 22-year-old workman was admitted to our hospital on May 6, 1966, with a complaint of shortness of breath and cough. His father, who died of hepatic cirrhosis at the age of 54, had a similar body habitus. He suffered from arthritis of the left foot at the age of 14. Inguinal hernia was repaired surgically at the age of 16 years. He was operated upon for right and left ectopic lentis at the ages of 17 and 19, respectively. A chest deformity was noticed at the age of 13 years, when he had palpitation and breathlessness on exercise. He became susceptible to colds with delay in recovery. At the age of 21, he suffered from paroxysmal dyspnea associated with common cold. There was no chest pain or edema except for visual disturbance until admission.

Physical findings :

He was slender (Fig. 5) ; the body height was 172 cm. and the weight 42 Kg. His pulse was 72/min. with a regular rhythm. The blood pressure was 118/60 mm.Hg. A significant degree of pectus excavatum with slight kyphoscoliosis was apparent.

An apical impulse was visible in the 6th intercostal space on the midclavicular line. Systolic thrills were present at the apex and in the 4th intercostal space along the left border of sternum.

Auscultation revealed a loud, grade 4-5/6, systolic murmur with intensified third sound over the area from the 4th intercostal space to the apex. There was a rough, grade 3/6, systolic murmur with a marked accentuation of the second sound

Fig. 5. Demonstration of arachnodactyly in Case 2.

Fig. 6. A chest X-ray film showing straightening of left cardiac waist and left ventricular enlargement.

over the pulmonic and Erb's area. A grade 2/6 systolic murmur which was transmitted to the left back was audible as well. No rales were audible in the lungs.

Chest X-ray films showed enlargement of the left ventricle and of the inferior portion of the right cardiac contour (Fig. 6). Bone X-ray films showed only an evidence of arachnodactyly.

Electrocardiogram revealed a pattern of the W.P.W. syndrome with a prominent delta wave at the beginning of QRS. PQ and QRS intervals were 0.12 and 0.16, respectively (Fig. 7).

Phonocardiogram showed pansystolic regurgitant murmur along the left lower border of the sternum and over the apex with intensified third sound. There was also systolic ejection murmur in the pulmonic and Erb's area. The second sound in the pulmonic area was slightly split (Fig. 8). Considerable decrease of the systolic

Fig. 7. The left electrocardiogram indicates the W.P.W. syndrome. The right shows pseudonormalized electrocardiogram with a first degree A-V block, after injection of ajimaline. 1mV. is 0.5 cm. in all leads but lead I of the left electrocardiogram, where 1mV. is 1cm.

Table I. Values of Cardiac Catheterization

	Pressure (mm.Hg)	Oxygen saturation (%)
Superior vena cava	9.0	79
Right atrium	8	85
Right ventricle	43/8	{88 86
Pulmonary artery	43/18	90
Pulmonary capillary	22	
Pulmonary vein	20	95
Left atrium	25	95
Aorta		93
Cardiac output	4.3 ml./min./M. ²	
Stroke volume	89 ml.	
Systemic flow	4.8 L./min.	
Pulmonary flow	6.4 L./min.	
% L-R shunt	25%	
Left atrial pressure mm.Hg		
a-wave	21	
c-wave	19	
v-wave	47	
x-descent	18	
y-descent	13

Fig. 8a. Phonocardiograms.

Fig. 8b. Phonocardiograms.

murmur along the left sternal border of the 4th intercostal space was observed immediately after the inhalation of amyl nitrite.

The results of cardiac catheterization is listed in Table I. Intracardiac pressure tracing of the left atrium demonstrated the presence of mitral insufficiency (Fig. 9). Angiocardiography was abandoned because of paroxysmal supraventricular tachycardia during catheterization (Fig. 10).

Laboratory findings :

Hemoglobin 41 % ; red cells 4.3 million ; white blood cells 8,800. Urinalysis showed no abnormalities. Erythrocyte sedimentation rate was 7 mm./hour. Total serum protein was 6.4 Gm./100 ml. with 69.8% albumin, 10.8% α -globulin, 10.3% β -globulin and 9.1% γ -globulin. Serologic studies revealed a weak positive CRP, 50 titers of ASLO and negative syphilitic reaction. Blood culture was negative.

DISCUSSION

In both cases the diagnosis of Marfan's syndrome was evident because of the presence of a marked dolichostenomelia with various bone deformities.

Fig. 8c. Phonocardiograms. See text.

- Ap: Apex
- A: Aortic area
- P: Pulmonic area
- Erb: Erb's area
- 5L: The 5th intercostal space along the left border of sternum
- 1: Medium-low pass filter
- 3: Medium-high pass filter

In the second case there were also ectopia lentis and cardiovascular abnormalities, namely the triad of Marfan's syndrome.

In the first case the presence of ventricular septal defect was suspected from the heart murmur prior to autopsy, but postmortem examination failed to demonstrate this combination. A marked displaced heart due to kyphoscoliosis or mitral insufficiency was presumed to be the cause of the murmur.

As for the cardiac abnormalities in the second case, the presence of mitral insufficiency was diagnosed from the above-mentioned characteristics of the phonocardiogram and of the atrial pressure curve in cardiac catheterization. The association of atrial septal defect could be diagnosed because the catheter

Fig. 9. The intracardiac pressure of left atrium showing predominant v-wave (the upper trace).

Fig. 10. The tip of catheter is observed passing from right atrium to left atrium.

tip could pass from the right atrium to the left atrium at that time, although the fixed splitting of P_2 was not apparent in the phonocardiogram, right bundle branch block was not noticed in the pseudonormalized electrocardiogram, and thrill was conspicuous in the pulmonic area. Whether there was in addition a ventricular septal defect or not was difficult to be determined. Even though there was the third sound and the decrease of murmur after administration of amyl nitrite in the phonocardiogram in Erb's area and at the apex, its significance was debatable because the diagnosis of mitral insufficiency was made already. Considering that similar murmur in the first case was not due to the ventricular septal defect, this finding in the second case might have been due to kyphoscoliosis. However, the cardiac catheterization revealed a significant difference in the oxygen content between the right ventricular blood and pulmonary artery blood, which supported its presence.

Relatively a few cases of Marfan's syndrome have been described to be associated with subacute bacterial endocarditis.^{2), 3)} Causative bacterial agents reported were streptococcus viridans in 4 cases, *Escherichia coli* and a Gram-positive streptococcus each in one case, and undetermined in 3 cases. In our first case, it was streptococcus viridans. Four such cases have been reported to be associated with subacute bacterial endocarditis in Japan. All of these cases were found to be associated with ventricular septal defect.

There have been numerous descriptions on electrocardiographic findings of Marfan's syndrome. A recent review by Bowers⁴⁾ included an extensive survey. In 63 cases of Marfan's syndrome listed in this article as well as in other previous reports, not a single case of the W.P.W. syndrome was men-

tioned.

To our knowledge, our second case is the first case of Marfan's syndrome associated with the W.P.W. syndrome. The W.P.W. syndrome in this case seemed to be congenital in origin, because the patient was told that he had an abnormal electrocardiographic pattern at puberty. In any case, it seems to be reasonable to assume that the combination of the W.P.W. syndrome and Marfan's syndrome is coincidental, because either the combination of congenital septal defect and Marfan's syndrome or that of congenital septal defect and the W.P.W. syndrome has been considered to be coincidental as well.⁵⁾

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