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Infective Endocarditis in a Patient with Williams' Syndrome
— Case Report —

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An 18-year-old male was admitted to Seoul National University Hospital for the evaluation of fever and chill on February 3, 1988.

On physical examination, his face showed a characteristic "elfin" facial appearance. His face was characterized by abnormalities of dental development, a broad overhanging upper lip, high arched palate and gum hypertrophy. He also showed mental retardation.

Cardiac catheterization with selective cineangiocardiography demonstrated a supravalvular aortic narrowing, grade 2 aortic insufficiency, and moderately dilated proximal coronary arteries with normal distribution without an intraluminal narrowing. There was a systolic pressure gradient (55mmHg) between the aortic root and ascending aorta distal to a stenotic segment.

MRI showed a supravalvular aortic stenosis.

Vegetation was not found on echocardiograpghy. Unidentified G(−) rods were isolated in 3 out of 9 bottles in blood culture test.

He was treated with Na-penicillin and gentamicin for 28 days.

Key Words: *Williams' syndrome, Supravalvular aortic stenosis, Endocarditis*

INTRODUCTION

Williams syndrome is characterized by the triad: supravalvular aortic stenosis, mental retardation and elfin facies.

doctor Williams first reported this syndrome in three females and one male-aged 7, 7, 12 and 11 years in 1961. Recently, we met an 18-year-old male with Williams syndrome and infective endocarditis presenting as fever and chill.

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Although several cases of Williams syndrome have been reported in Korea, an adult patient with Williams syndrome, especially associated with infective endocarditis, has not been reported.

This paper presents a case report of adult Williams syndrome with infective endocarditis.

CASE REPORT

An 18-year-old male was admitted to Seoul National University Hospital for the evaluation of fever and chill. He was relatively well until 20 days prior to admission when intermittent fever and chill developed he had his teeth extracted. For 3 days prior to admission, he also suffered from abdominal pain and frequent loose stool.

He was admitted through the emergency room for further evaluation.

His past history was not contributory except for frequent episodes of upper respiratory infections shince childhood. In all the family members, including parents and 2 brothers, evidence of congenital anomaly or mental retardation was not found. The patient was a high school student and his parents said he was poor in academic achievement.

On physical examination he had a peculiar facial appearance. He was 158.2 cm tall and weighed 41 Kg. His body temperature was 37.5°C and respiratory rate was 20 per minute. His blood pressure was 150/90mmHg in the right and 130/80 mmHg in the left arm. His facies showed a characteristic "elfin" facial appearance (Fig. 1). His face was characterized by abnormalites of dental development, a broad overhanging upper lip, high arched palate and gum hypertrophy (Fig. 2). Ocular examination showed strabismus and epicanthic folds were absent.

Cardiac examination revealed a left precordial lift. A systolic thrill was palpable in the suprasternal notch and along the carotid vessels. The second heart sound was accentuated. A grade 4 (on the basis of 6) systolic ejection murmur was heard maximally over the right and left upper sternal borders and radiated into the suprasternal notch and along the carotid vessels. A grade 3 early diastolic, decrescendo, blowing murmur was heard maximally over the Erb's area. Aortic ejection click was absent. The liver was palpable 2 finger breadths below the costal margin. Its surface was soft and tender.

The hemogram revealed hemoglobin 9.1g/dl (MCV 81.0, MCH 27.9, MCHC 34.5), WBC count 10300/mm3, platelet count 291000/mm3 and ESR 125mm/hr. The admission tests showed calcium 8.2g/dl, Phosphorous 3.5g/dl, BUN 6 mg/dl, creatinine 1.0mg/dl, uric acid 2.6mg/dl, albumin 3.2g/dl, bilirubin 0.3mg/dl, alkaline phosphatase 88 IU/1, SGOT 8 IU/1, SGPT 8 IU/1, sodium 139mmol/1, potassium 4.4mmol/1 and chloride 103 mmol/1. Urinalysis showed pH 7,specific gravity 1.005, albumin trace, blood +++ and microscopic hematuria. Prothrombin time was 66% (100-80%) and activated PTT was 37 seconds (30-45 seconds). The ASO titer was negative, CRP 6 positive, RA factor negative, VDRL non-reactive, IgG 3320 mg/dl

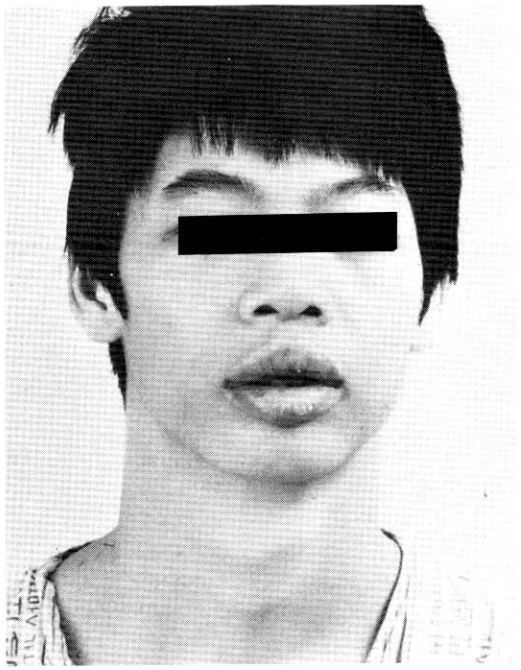

Fig. 1. *A characteristic "elfin" facies. Note a broad overhanging upper lip.*

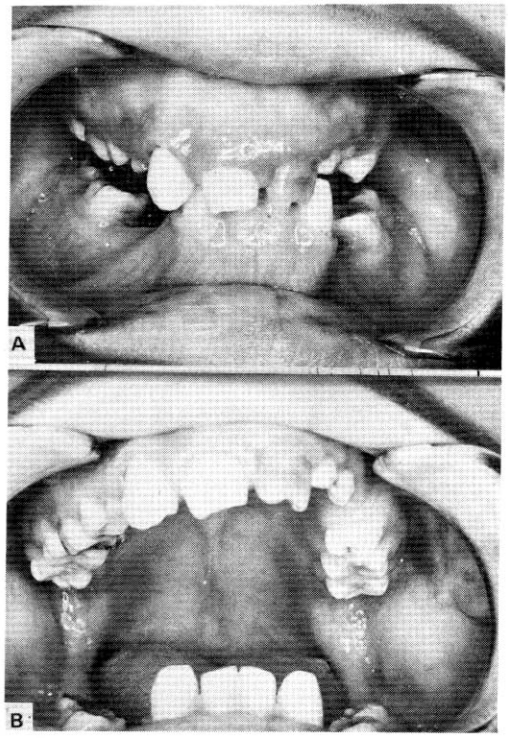

Fig. 2. *(A) Note abnormalities of dental development and gum hypertrophy.*
(B) Note a high arched palate.

(408-1788), IgA 634 mg/dl (64-544) and IgM over 483mg/dl (49-355). Iron was 62 ug/dl (50-170) and TIBC 252 ug/dl (280-400).

On blood culture, unidentified G (−) rods (anaerobe) in 3 out of 9 bottles were isolated. Roentgenologic examination revealed normal heart size, pulmonary vascularity, no acitve lesion in the lung and lack of poststenotic dilatation of the aorta (Fig. 3). An electrocardiogram showed nonspecific ST-T

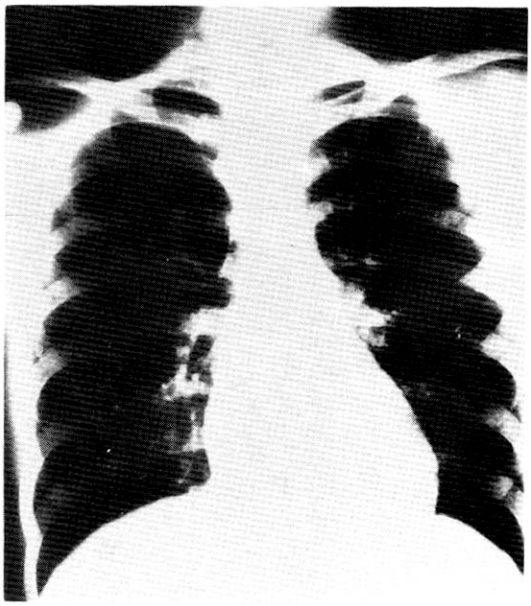

Fig. 3. *Roentgenogram of chest showing a normal heart size. No distinct poststenotic dilatation of the aorta is seen.*

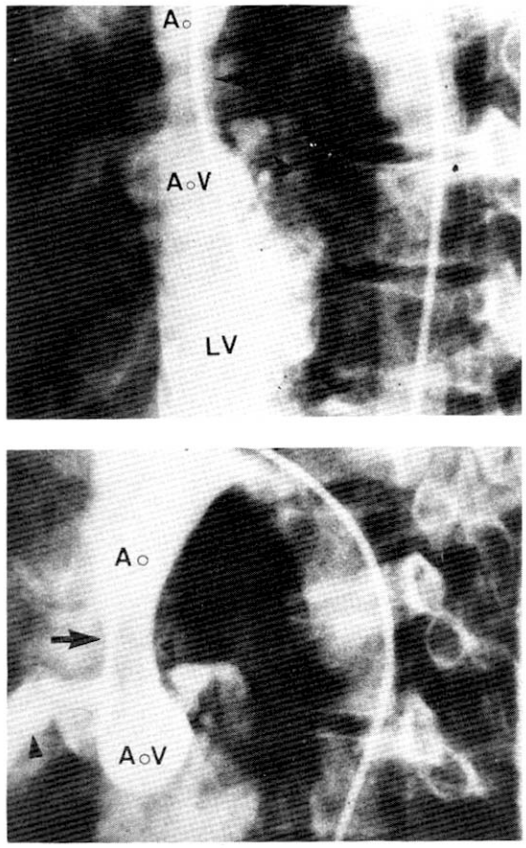

Fig. 4. *A) Left ventriculography B) Aortography Angiocardiograms show that the supravalvular aortic stenosis, hour glass type (arrow), is clearly shown above the aortic valve. Note moderately dilated right and left coronary arteries (arrowhead). LV = left ventricle; Ao = aorta; AoV = aortic valve.*

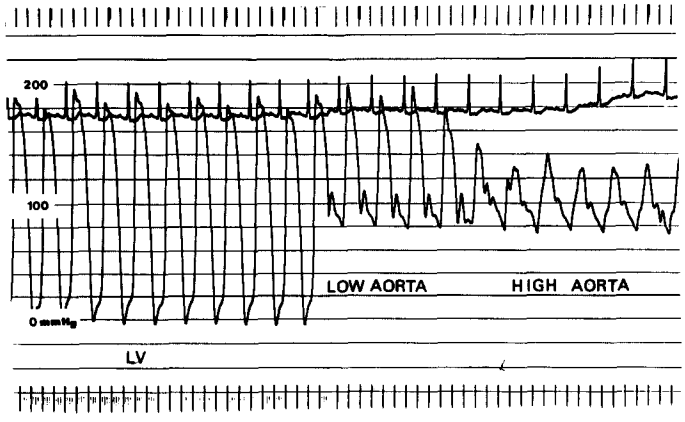

Fig. 5. *Pressure tracing showing that the systolic gradient marking the site of stenosis lies above the aortic valve.*

changes.

An echocardiography showed normal chamber size, normal aortic valve leaflet and aortic insufficiency on Doppler with no vegetation.

Cardiac catheterization with selective cineangiocardiography was performed. A cineangiography with the catheter in the ascending aorta distal to the aortic valve demonstrated a supravalvular aortic narrowing (Fig. 4) and grade 2 (on the basis of 4) aortic insufficiency. There was a peak to peak systolic pressure gradient of 55mgHg between the aortic root and ascending aorta distal to a stenotic segment (Fig. 5). Using all available coronary catheters, coronary arteriography was attempted but failed. Aortic root angiography showed moderately dilated proximal coronary arteries with normal distribution without an intraluminal narrowing (Fig. 4). There was no pulmonary hypertension. A chromosome assay showed a 46 XY.

Magnetic resonance imaging (MRI) showed a supravalvular aortic stenosis (Fig. 6).

He was treated with Na-penicillin and gentamicin for 28 days. In 3 days he became afebrile and after the completion of treatment an urinalysis showed 1-2 RBC/HPF. CRP was weakly reactive and ESR was 71 mm/hr.

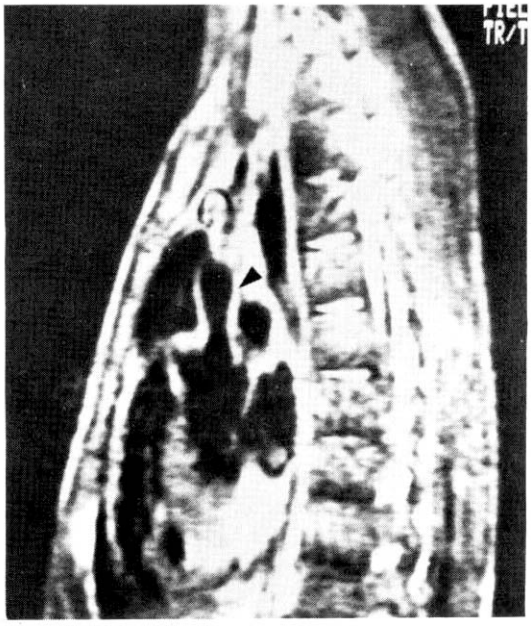

Fig. 6. *Left lateral magnetic resonance image demonstrating a supravalvular aortic stenosis (arrowhead).*

He was transferred to the thoracic surgery ward for an operation.

DISCUSSION

Williams syndrome is characterzed by the triad: supravalvular aortic stenosis (AS), mental retardation and elfin facies. In addition, mild microcephaly, neurologic dysfunction, auditory hyperacusis, narrowing of the peripheral systemic and pulmonary arteries, inguinal hernia, strabismus, abnormities of dental development, epicanthal folds, high prominent forehead, and an overhanging upper lip may be present[1-3]. Rarely, mitral valve abnormalities with prolapse, mitral regurgitation, PDA, subaortic membrane, ASD, VSD and COA may be accompanied.[4]

Peripheral pulmonary artery stenosis and aortic anomaly are also seen in familial and sporadic forms unassociated with the other features of the syndrome.

Three anatomical types of supravalvular AS are recognized. The most common is the hourglass type, in which marked thickening and disorganization of the aortic media produce a constricting annular ridge at the superior margin of the sinuses of Valsalva. The membranous type is the result of a fibrous or fibromuscular semicircular diaphragm with a small central opening stretched across the lumen of the aorta. Uniform hypoplasia of the ascending aorta characterizes the hypoplastic type.

Those with the familial form usually have a distinctive family history in which parents or siblings have documented supravalvular AS. Genetic studies suggest that the familial anomaly is transmitted as an autosomal dominant trait with variable expression. Unlike the other forms of aortic stenosis, there appears to be no sex predilection. Supravalvular aortic stenosis may rarely be the result of congenital rubella. The typical appearance is similar to the elfin facies observed in the severe form of idiopathic infantile hypercalcemia.

The pathogenetic mechanism of the syndrome is not yet established.

Experimental hypervitaminosis D produced in the pregnant rabbit has caused craniofacial abnormalities and malformations resembling those of supravalvular aortic stenosis in the offspring. The hypothesis of hypercalcemia resulting from abnormal regulation of circulating 25-hydroxyvitamin D in Williams syndrome has been reported.[5-6]

In humans, with one exception, chromosome studies have consistently revealed normal karyotypes.

The symptoms of supravalvular AS are similar to those of valvular and subvalvular AS, although critical obstruction with congestive heart failure in the neonatal period is exceedingly rare. Growth and development usually are normal. Easy fatigue, dyspnea, syncope or angina suggest severe obstruction in the case of a supravalvular AS, but severe obstruction may exist in the absence of any symptoms. Those with a characteristic face and mental retardation usually have a history of irritability, vomiting and hypotonia in early life, an observation lending support to the hypothesis of hypercalcemia.

With few exceptions, the major physical findings resemble those observed in patients with valvular AS. Among these exceptions are accentuation of the aortic valve closure due to elevated pressure in the aorta proximal to the stenosis, an infrequent systolic ejection sound, and the particularly prominent transmission of a thrill and murmur into the jugular notch and along the carotid vessels. Uncommonly, there is an early diastolic, decrescendo, blowing murmur of aortic regurgitatioin due to the fusion of one or more cusps to the area of stenosis. A systolic blood pressure difference may be recorded between the two arms on occasion; the systolic pressure in the right arm tends to be the higher of the two and occasionally exceeds that in the femoral arteries. The disparity in pressures may be related to the tendency of a jet stream to adhere to a vessel wall (Coanda effect) and selective streaming of blood into the innominate artery.[7]

Because the coronary arteries arise proximal to the site of outflow obstruction in supravalvular aortic stenosis, they are subjected to the elevated pressure that exists within the left ventricle. These vessels are often dilated and tortuous, and premature coronary arteriosclerosis has been observed.

Radiologically, in contrast to valvular and discrete subvalvular aortic stenosis, poststenotic dilation of the ascending aorta is rarely seen. Electrocardiography reveals left ventricular hypertrophy when obstruction is severe. However, biventricular or even right ventricular hypertrophy may be found if significant narrowings of peripheral pulmonary arteries coexist.

Echocardiographically the M-mode technique may demonstrate the narrowed diameter of the aortic lumen just distal to the aortic valve. However, the two dimensional technique visualizes this much more clearly and permits an estimation of the degree of severity in terms of both the narrowing of the aortic lumen and the extent of the ascending aortic involvement. Doppler echocardiography acts synergistically with ultrasound imaging to provide a noninvasive estimate of pressure gradients in patients with supravalvular AS.

The pulsed Doppler technique allows localization of the level of obstruction. This is particularly important in differentiating between subvalvular, valvular and supravalvular stenoses. Continuous wave Doppler allows accurate quantitation of peak instantaneous and mean systolic gradients across the level of obstruction.

Magnetic resonance imaging has also been used successfully to diagnose supravalvular AS lesion.[8]

A systolic pressure gradient can be demonstrated just above the aortic valve by careful pullback pressure tracings from the left ventricular cavity to the aortic arch.

Supravalvular aortography or left ventricular angiography will visualize the supravalvular narrowing. Pressure recordings in the branch pulmonary arteries should be obtained and right ventricular or pulmonary arterial angiography should be performed in the presence of any significant right ventricular systolic pressure elevation, in order to rule out associated stenoses of the pulmonary arteries.

The sequences of progressive obstruction, the appearance of symptoms and electrocardiographic changes, and the possibility of sudden death appears to apply for supravalvular aortic stenosis as well as for valvular aortic stenosis.

Patients with supravalvular aortic obstruction appear to be subject to the same risks of unexpected sudden death and infective endocarditis.[9]

The supravalvular aortic lumen may be widened by the insertion of an oval or diamond-shaped fabric patch in those patients with a normal ascending aorta.[4] If the aorta is markedly hypoplastic, this operation merely displaces the pressure gradient distally without abolishing the obstruction.

Under these circumstances, repair may require replacement or widening of the entire hypoplastic aorta with an appropriate prosthesis. Diffuse tubular hypoplasia of the ascending aorta is a technically challenging problem associated with a high mortality and poor postoperative hemodynamic results. A few patients will have severe pulmonary arterial stenoses which may or may not be amenable to repair, the presence of which may increase the risk of aortic surgery considerably.[10-11]

Operation may be recommended when relatively little hypoplasia of the ascending aorta and arch exists and when the obstruction is discrete and significant, i.e. with a systolic gradient exceeding 50

mmHg.

The parents of the patient with the familial variety of supravalvular AS with mental retardation will benefit from genetic counselling regarding contraception for the retarded adolescent female.

SUMMARY

A 18-year-old male with supravalvular aortic stenosis, mental retardation and peculiar elfin facies is described. To our knowledge, this represents the first case report of Williams syndrome with infective endocarditis.

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