

Ruptured Aneurysm of the Sinus of Valsalva With Wildervanck Syndrome (Cervico-Oculo-Acoustic Syndrome), Blepharoptosis and Short Stature

— Case Report —

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A 62-year-old woman was admitted to hospital because of nausea. A grade 5/6 continuous murmur was audible near the left sternal border at the second intercostal space. Chest X-ray showed cardiomegaly and bilateral pleural effusion. She was diagnosed as heart failure and a diuretic was prescribed. After remission of the heart failure, echocardiography showed shunt flow from the right coronary cusp to the right ventricle. Aortography revealed that an aneurysm of the right coronary sinus of Valsalva had ruptured into the right ventricle. Coronary angiography revealed a single coronary artery. Chest computed tomography revealed persistent left superior vena cava. Surgical repair was carried out and the patient made an uneventful recovery. In addition to these cardiovascular abnormalities, she had Wildervanck syndrome (Klippel-Feil syndrome, Duane syndrome and sensorineural hearing disturbance), blepharoptosis and short stature. This rare combination has not been reported previously. (Circ J 2007; 71: 1485–1487)

Key Words: Aneurysm; Ptosis; Sinus of Valsalva; Wildervanck syndrome

Aneurysm of the sinus of Valsalva (ASV) is frequently associated other congenital heart disease, but there has not been a previous report describing Wildervanck syndrome (cervico-oculo-acoustic syndrome) accompanying ASV. We present, for the first time, such a case. Any unknown syndrome may account for this rare combination.

Case Report

A 62-year-old woman was admitted to hospital because of nausea. On admission, her height was 120 cm, body weight was 34.0 kg, and blood pressure was 124/76 mmHg. She had edema of the face and feet. A grade 5/6 continuous murmur was audible near the left sternal border at the second intercostal space. Chest X-ray showed cardiomegaly and bilateral pleural effusion. Electrocardiography showed sinus tachycardia, right axis deviation, and clockwise rotation. Plasma level of brain natriuretic peptide was 1,400 pg/ml. She was diagnosed as having heart failure and a diuretic was prescribed. After remission of the heart failure, echocardiography was performed and revealed shunt flow from the right coronary sinus to the right ventricle (Fig 1). The wall motion of the left ventricle and the dimen-

sions of the right ventricle were normal. Cardiac catheterization was performed; right-heart catheterization indicated elevated pressure in the pulmonary wedge, pulmonary artery, right ventricle and right atrium, as well as right ventricular outflow obstruction (Table 1). Right ventriculography showed dilatation of the proximal pulmonary artery, and left ventriculography showed normal wall motion of the left ventricle and no apparent ventricular septal defect. Aortography revealed an aneurysm of the right coronary sinus of Valsalva that had ruptured into the right ventricle,

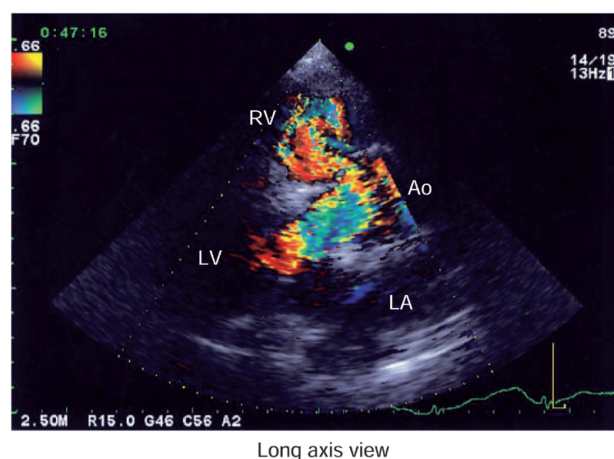


Fig 1. Two-dimensional and color Doppler echocardiography shows shunt flow from the right coronary cusp to the right ventricle. RV, right ventricle; LV, left ventricle; LA, left atrium; Ao, aorta.

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Table 1 Cardiac Catheterization Data

Chamber	Pressure (mmHg)	Oxygen saturation (%)
Superior vena cava	—	58
Inferior vena cava	—	70
Right atrium	17/13 (mean 14)	64
Right ventricle (apex)	90/40 (EDP 25)	76
Right ventricle (outflow)	59/20	—
Pulmonary artery	53/22 (mean 35)	84
Pulmonary artery wedge	26/3 (mean 19)	97
Left ventricle	—	—
Femoral artery	94/35	94

Cardiac index = $6.51 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$; heart rate 80 beats/min; $Q_p/Q_s = 2.3$; ratio of left to right shunt 61%.



Fig2. (Upper) Note the bilateral blepharoptosis and convergent strabismus. (Lower) Note the lower occipital hairline (arrow).

and mild aortic regurgitation. Aortography showed no apparent patent ductus arteriosus. Coronary angiography revealed a single coronary artery. Blood gas sampling indicated a step up of oxygen saturation at the right ventricle and pulmonary artery. The pulmonary to systemic flow ratio was 2.3 and the rate of left-to-right shunt was 61%. Chest computed tomography revealed a persistent left superior vena cava. Direct closure of the aneurysm of the right coronary sinus was performed and the patent foramen ovale detected by intraoperative transesophageal echocardiography was also closed. Fenestrations of 3 aortic cusps were detected and closed. The postoperative course was uneventful.

In addition to these cardiovascular abnormalities, the patient had congenital myopia, bilateral ptosis and convergent strabismus (Fig 2), and her eyes had limited abduction (Fig 3). She showed severe sensorineural hearing disturbance on audiometry (mean hearing level: right 73.8 dB, left 26.3 dB). She had a short neck and a low occipital hairline (Fig 2). Vertebral X-rays showed adhesion of C5–6



Fig4. Cervical vertebral X-ray showing fused cervical vertebrae (C5–6).

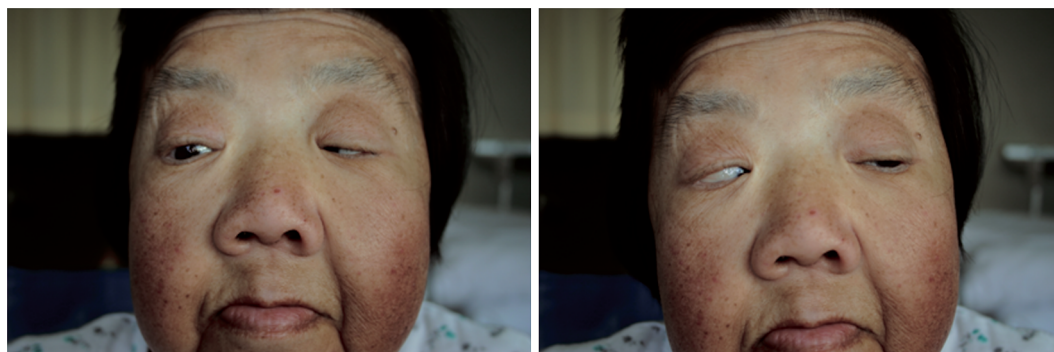


Fig3. Bilateral abducens palsy, shown during looking to right and to left.

(Fig 4) and kyphoscoliosis. Her fingers were normal. From these findings, we made a diagnosis of ASV accompanying Wildervanck syndrome (cervico-oculo-acoustic syndrome) which consists of Duane syndrome (abducens palsy with retraction bulbi), Klippel-Feil syndrome and congenital sensorineural hearing disturbance.

She had undergone 5 spontaneous abortions and 1 delivery by caesarian operation. Gynecological examination revealed no abnormality. Her parents were not consanguineous and had no apparent cardiovascular disease. She had no siblings. Her daughter was healthy and presented no physical abnormality. After we obtained informed consent, her chromosomes were screened by G-band and revealed that chromosomes in 4% of cells were 45X and 96% were 46XX.

Discussion

We present, for the first time, a patient with Wildervanck syndrome accompanied by various cardiovascular abnormalities including ASV, blepharoptosis and short stature. It may be helpful to begin with a discussion of the underlying cause of Wildervanck syndrome to examine this rare combination.

Although the mechanism of Wildervanck syndrome is unknown, the overwhelming preponderance of female cases has led to the conjecture that the disorder is X-linked dominant with lethality in males.¹ There has been no report of chromosomal aberrations in Wildervanck syndrome, and the small percentage of 45X observed in the chromosomes of this patient are probably age-associated aneuploidy.² Wildervanck syndrome consists of Klippel-Feil syndrome, Duane syndrome, and congenital sensorineural hearing disturbance. Recent molecular genetic studies have suggested that Klippel-Feil syndrome may result from mutations or disruption of genes regulating segmentation, such as PAX1,³ SGM1,⁴ and FGFR3.⁵ Vertebral segmentation occurs between the 4th and 8th weeks of gestation and any impairment in differentiation of the mesoderm may relate not only to cervical abnormalities but also to the combination of rare cardiovascular abnormalities such as ASV, single coronary artery, persistent left superior vena cava, patent foramen ovale and aortic valve fenestration observed in this patient. In fact, Klippel-Feil syndrome is associated with various cardiovascular abnormalities in 4–29% of patients.⁶ There have been 2 case reports of ASV with Klippel-Feil syndrome,^{7,8} which supports the conjecture of an underlying mechanism of coexistence of these rare cardiovascular

anomalies in the present patient.

In addition to the various cardiovascular abnormalities, our patient showed blepharoptosis and short stature, which have not been reported as associated with Wildervanck syndrome. In a large series of patients with congenital heart disease, blepharoptosis was reported as 0.96%, almost 20-fold that of the control population.⁹ Larned et al speculated that an environmental influence acting between the 5th and 8th weeks of gestation might affect the development of muscle fibers in both the heart and the orbit,¹⁰ so any impairment in differentiation of mesoderm at that time may relate to the blepharoptosis and various cardiovascular anomalies of the present patient. Regarding the combination of blepharoptosis and short stature, Sonoda et al reported 12 cases of congenital heart disease with ptosis and short stature without chromosomal aberration nor recognizable malformation syndromes such as Noonan syndrome or mitochondrial encephalomyopathy.¹¹ Further studies are necessary to clarify whether an unknown syndrome may account for this rare combination.

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