Complete Transposition of the Great Arteries with Large Ventricular Septal Defect and Pulmonary Hypertension: Progressive Pulmonary Vascular Disease after Total Correction

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YAMAKI, S., HIRIUCHI, T., MOHRI, H., ISHIZAWA, E., KOIZUMI, S., KAHATA, O., YOKOYAMA, A., ARAKI, J., OHMI, M. and FUKUDA, M. Complete Transposition of the Great Arteries with Large Ventricular Septal Defect and Pulmonary Hypertension: Progressive Pulmonary Vascular Disease after Total Correction. Tohoku J. exp. Med., 1979, 127 (3), 201-207 — The postoperative change in pulmonary vascular disease following complete surgical repair in cases of the complete transposition of the great arteries with severe pulmonary hypertension remains an extremely interesting problem. We have performed complete surgical repair on an 8-month-old boy with severe pulmonary hypertension having a pulmonary-systemic pressure ratio of 1.0 and 14 units of pulmonary vascular resistance, but who suddenly died 9 months postoperatively. The results of a comparison of the histometrical measurements of biopsy lung and autopsy lung showed postoperative hypertrophy of the media of the small pulmonary arteries and progressed pulmonary vascular disease. It is thought that this phenomenon was brought about in the following way: The specific factor in this congenital heart disease which suppresses the hypertrophy of the pulmonary arterial media is removed due to the total correction and the media over-reacts to the postoperative pulmonary arterial pressure, resulting in hypertrophy. Repeated vasoconstriction of the abnormally thick pulmonary arterial walls leads to ischemic change in the peripheral blood vessels and obstructive pulmonary vascular disease is progressively brought about. —— pulmonary hypertension; progressive pulmonary vascular disease; index of pulmonary vascular disease; histometrical analysis of pulmonary arterial wall

It is a well known fact that pulmonary vascular disease (PVD) develops from an early period in complete transposition of the great artery (TGA) with large ventricular septal defect (VSD).

We have recently undertaken total correction in a case of TGA with a large VSD in which severe pulmonary hypertension was seen, but who died suddenly in a

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late postoperative period. We have made a comparative analysis of the pre-
and post-operative PVD based upon histological and histometrical measurements.
Here we report confirmation of progressive PVD and discuss some interesting
findings which bear on the mechanism of pathogenesis.

CASE REPORT

An 8-month-old boy was admitted to the Tohoku University Hospital on
February 16, 1977, with deep cyanosis and physical retardation. A heart
murmur and cyanosis were apparent immediately following delivery, so that
cardiac catheterization was performed 19 days from birth. He was diagnosed as
TGA with a large VSD and balloon atrial septostomy was performed.

On admission the patient was 5690 g in weight and 65 cm in height with
severe cyanosis of the lips and nail beds. Blood pressure at the upper limbs was
100/72 mmHg and pulse rate was 140/min, the liver was palpable 4 fingers
breadth below the right costal margin. A harsh systolic murmur (Levine III) was
audible at the left sternal border. Red blood cell count was 784×10^4/mm³,
hemoglobin was 15.1 g/100 ml, hematocrit was 54.1%, and polycythemia was
identified. Chest x-ray film revealed pulmonary congestion and marked
cardiomegaly (cardio-thoracic ratio, 70%). An electrocardiogram showed sinus
rhythm and right ventricular hypertrophy. The results of cardiac catheterization
showed similar pulmonary arterial pressure and aortic pressure of 88/56 (70) mmHg
and 86/56 (70) mmHg, respectively, 14 units of pulmonary vascular resistance, a
pulmonary-systemic resistance ratio of 0.9, and a pulmonary flow of 4.5 liter/min/m².
Angiography showed the aorta originating from the right ventricle and the
pulmonary artery trunk originating from the left ventricle, as well as the presence
of a large VSD. From the above findings, this case was diagnosed as TGA with a
large VSD and severe pulmonary hypertension; the hemodynamic values suggested
that the total correction would be impossible.

The operation was performed on March 1, 1977. After bringing the throat
temperature to 28°C by surface cooling, the heart was approached by way of
median sternotomy and lung biopsy was performed. The biopsy lung showed an
index of pulmonary vascular disease (IPVD) of 2.26 (Yamaki 1977a; Yamaki and
Tezuka 1978) which is near the upper limit for radical surgical therapy.
Consequently, it was decided to undertake the Mustard operation and closure of
the VSD. Using core cooling, a throat temperature of 17°C was obtained,
circulatory arrest begun, and a transverse incision from the right atrial appendage
to the left atrium performed. The VSD (5 mm in diameter) was closed using a
Teflon patch from the atrial side and the Mustard operation was performed using a
prefabricated Dacron baffle (Dillard et al. 1977; Ohmi et al. 1977). The
cardiopulmonary bypass time, including the total circulatory arrest time, was 110
min. The measurement of blood pressures immediately following the operation
showed almost no fall in the pulmonary arterial pressure, aortic pressure being
95/40 (60) mmHg and pulmonary arterial pressure being 90/30 (50) mmHg.
Though a respirator (RPR) was used from the beginning of intensive care, desaturation was evident. This was thought to be due to a large shunt from the pulmonary circulation to the systemic circulation through the prefabricated Dacron baffle used in the Mustard operation. The hypoxemia began to gradually improve 9 days postoperatively and disappeared 2 weeks from surgery. Throughout the postoperative period, no symptoms of marked congestive heart failure were seen. At this point weaning from the respirator was attempted, but, due to respiratory failure, respiratory care was necessary for 40 days.

Thereafter, a cardio-thoracic ratio of 63% was seen, indicating reduced cardiomegaly as compared with the preoperative condition. Since the liver was no longer palpable and he had a good appetite and was comfortable, he was discharged 4 months postoperatively. At that time, the polycythemia had improved. However, 9 months postoperatively he developed a cough, his face grew pale with rapid breathing, cyanosis increased and he suddenly died.

**Autopsy findings.** The patient had a body weight of 7 kg and a height of 73 cm. The VSD had been completely closed and the Teflon patch had become organized. There was no stenosis of the superior or inferior vena cava and pulmonary venous obstruction due to the baffle was not seen, indicating that the Mustard operation itself had been successful. Other than findings concerned with the cardiovascular system, congestion of the hilus of the lungs was apparent. Intraabdominally, ascites was not seen, but the liver had enlarged to 320 g. The spleen, kidney and gastrointestinal system were, however, normal.

**Histometrical results.** From the histological findings of the biopsy lung (Fig. 1) and autopsy lung (Fig. 2), it appeared that hypertrophy of the pulmonary arterial wall had occurred after complete surgical repair. Therefore, a histometrical
analysis was made of the postoperative change of the medial thickness in small pulmonary arteries. Suwa's method (Suwa and Takahashi 1971) was utilized for measuring the thickness of the pulmonary arterial media to examine precisely the magnitude of this postoperative hypertrophy. As a result, it was found that postoperatively the muscular pulmonary arterial walls had hypertrophied as roughly twice as their preoperative thickness (Fig. 3).

Since progressive pulmonary vascular disease was suggested from the postoperative lung sections (Fig. 4), the severity of the PVD was analyzed from biopsy and autopsy lung using the IPVD method previously published by the authors (Yamaki 1977a, Yamaki and Tezuka 1978). A total of 644 pulmonary arterial branches from the serial sections of biopsy lung was examined and it was found that 151 showed a score of 1 (no intimal reaction), 275 had a score of 2

![Transverse section of a muscular pulmonary artery in autopsy lung specimen. Note the marked hypertrophy of the media.](image)

![Significant correlations were observed between radius (R) and medial thickness (D) of small pulmonary arteries in biopsy and autopsy lungs in a logarithmic coordinate system. The evaluation of the equation for biopsy lung was distinctly lower (p<0.001) than that for autopsy lung. •, autopsy lung D=1.169R^{0.412} (r=0.91, n=22); ○, biopsy lung D=0.890R^{0.461} (r=0.93, n=16).](image)
(cellular proliferation of the intima), 118 had a score of 3 (intimal fibroelastic proliferation), and 100 had a score of 4 (medial destruction). Consequently, the IPVD, the value obtained by dividing the total score by the number of pulmonary arterial branches, was 2.26. Since the biopsy lung was obtained from the left upper lobe, a total of 482 pulmonary arterial branches was taken from the same lobe of the autopsy lung and the severity of the pulmonary arterial vascular lesions was analyzed. Sixty-seven pulmonary arteries with score of 1, 99 with score 2, 227 with score 3, and 89 with score 4 were counted and an IPVD of 2.70 obtained.

Fig. 4. Pulmonary vascular disease in autopsy lung specimen. Note the destruction of the media.

Fig. 5. The percentage of pulmonary arterial branches with each score in biopsy and autopsy lungs.
indicating that the postoperative vascular lesions had developed to a severer state than preoperative condition. With regard to the percentage of each score, it was clearly seen that preoperative scores 1 and 2 had developed into scores 3 and 4, which indicated irreversible obstructive vascular lesions (Fig. 5).

**DISCUSSION**

In this patient, preoperative cardiac catheterization indicated that a radical operation would be impossible due to severe PVD as a result of pulmonary hypertension. However, since biopsy showed the grade of pulmonary vascular changes to be at the borderline of the critical limit for complete surgical repair, radical surgery was carried out. Pressure measurements performed immediately following surgery showed no marked decrease in pulmonary arterial pressure, suggesting likely congestive heart failure. However, a large shunt from the pulmonary circulation to the systemic circulation through the Dacron baffle used in the Mustard operation alleviated the postoperative congestive heart failure. Nevertheless, protracted respiratory failure appeared from a time 2 weeks postoperative when the shunt disappeared and it suggested the development of obstructive PVD. A comparative analysis of histometrical findings of the biopsy and autopsy lungs indicated marked development of the obstructive PVD postoperatively and it it believed to be the direct cause of death. Here, brief discussion will be made concerning the mechanism of the postoperative development of PVD in this patient.

Our histometrical research concerning the specificity of the pulmonary arterial wall in TGA using VSD as a control has been previously reported (Yamaki 1977b; Yamaki and Tezuka 1976). It had been found that when there is a rise in intraarterial blood pressure, the arterial media tends to hypertrophy to adapt to the increased blood pressure (Suwa and Takahashi 1971). In TGA, however, even when there is a rise in pulmonary arterial pressure, some specific factor suppresses the hypertrophy of the media. Consequently, the thickness of the media in TGA is only 70% that found in VSD at the same blood pressure level after 6 months from birth. The pulmonary arterial walls in TGA are, therefore, thin and weak, cannot sufficiently adapt to increased pulmonary arterial pressure, and easily succumb to severe PVD. Incidentally, it may be suggested that the factor suppressing medial hypertrophy in TGA is related to the unique hemodynamics of TGA. Since normal hemodynamics were achieved in this patient due to the radical operation, it is considered that the factor responsible for suppression of medial hypertrophy disappeared. Furthermore, since the pulmonary arterial pressure was maintained at a high level postoperatively, it is easy to understand that the media reacted to the pulmonary arterial pressure and quickly began to hypertrophy immediately following surgery, ultimately resulting in severe hypertrophy. As mentioned above, hypertrophy of the arterial wall is brought about as a functional adaptation to increased intraarterial blood pressure. Therefore, it may be considered that, due to the postoperative hypertrophy of the pulmonary
arterial media, the wall was sufficiently strong to be able to adapt to the high pulmonary arterial pressure and that PVD could not progress beyond that level. However, although strong, excessively hypertrophied arterial walls easily succumb to vasoconstriction due to only slight stimulation. Consequently, it is believed that the peripheral small pulmonary arteries were made ischemic due to the vasoconstriction and that repeated pulmonary vasoconstriction would cause endothelial stress and damage of the peripheral small arteries and ultimately the rapid development of obstructive vascular changes.

According to the reports of Newfeld et al. (1974), Rosengart et al. (1975), and Mair et al. (1973), as well, the development of PVD following radical surgery for TGA is not thought to be rare. Especially in cases of pulmonary hypertension, postoperative hypertrophy of the pulmonary arterial media would be unavoidable and cause frequent occurrence of vasospasms, ischemia of peripheral small pulmonary arteries, and be responsible for the development of severe PVD. Since hypertrophy of the pulmonary arterial media correlates with the magnitude of the pulmonary arterial pressure, in cases where postoperatively the pressure does not drop sufficiently, it is suggested that the prognosis is extremely poor due to the rapid development of these unfavorable phenomena outlined above.

References


