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## CASE REPORT

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# *XYX male with total anomalous pulmonary venous return and short stature*

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### Abstract

**Objective:** to report a case of a 47 XYX male neonate with congenital heart disease and short stature.

**Description:** this is the first case report of a 47 XYX male neonate associated with congenital heart disease (total anomalous pulmonary venous return) and small for gestational age. The infant was born at around 32 weeks of gestation with 1,134g. Intracranial hemorrhage and pulmonary high flow were discovered in the early neonatal period. Retarded physical and mental development was observed. The infant underwent a palliative ligation of the ductus arteriosus and a ventriculoperitoneal shunt operation, but died due to consequent heart failure at 19 months of age.

**Comments:** this combination of XYX male and congenital heart disease may be fortuitous. However, we think it is important to report that there was a poor prognosis case of XYX male with congenital heart disease and short stature.

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### Introduction

XYX syndrome is a chromosomal anomaly, in which subjects are considered to be relatively tall in stature. However, there are case reports of behavioral problems in some patients. There have been no known reports concerning XYX male with congenital heart disease and short stature in the literature.

### Case Report

A fetal echocardiogram carried out at the hospital showed intrauterine growth retardation and diastolic regurgitation

of the umbilical artery of the fetus. The subject's mother was urgently transferred to our hospital and asphyxia of the fetus appeared during a non-stress test and an emergency Cesarean section was performed. A male with short stature and with severe respiratory dyspnea and cyanosis was born, and was immediately intubated and admitted to the neonatal intensive care unit. His Apgar scores were four and eight at one minute and five minutes after birth, respectively. His body weight was 1,134 g (-2.3 SD: standard deviation-based on the statistics of Japanese infants), his height was 37.5 cm (-1.8 SD: same as mentioned above) and, as such, he was small-for-gestational age. However, his gestational age was not clear due to a lack of adequate, regular follow-up of the mother. Therefore, we estimated the infant to be approximately 32 weeks of gestation using the Parkin's method. He was the second child of Brazilian parents living in Japan. He had a narrow forehead, a projected intereyebrow

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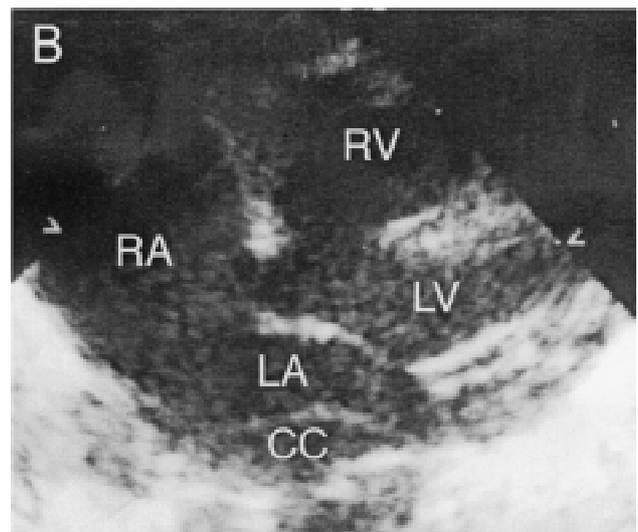
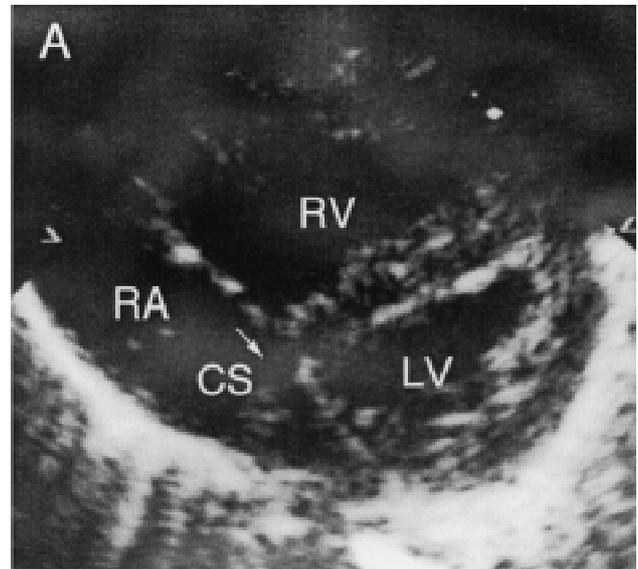
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area, a short nose with depressed nasal bridge, anteverted nares, large and low-set ear lobes, sparse hair, and scant eyebrows. (Figure 1), but did not have macrocephaly, ptosis, high-arched palate, hyperkeratosis, hypospadias, or retained testicles. Doppler echocardiography with color flow imaging revealed situs solitus, levocardia, total anomalous pulmonary venous return type IIa, atrial septal defect, ventricular septal defect, persistent ductus arteriosus and no pulmonary stenosis (Figure 2). Nonetheless, no anomalous findings were detected by cranial ultrasound or routine laboratory examinations. A chromosomal examination revealed that his karyotype was 47 XYY. Pulmonary stenosis of the pulmonary valve (pressure gradient was 23 mmHg) appeared at about one week of birth. His respiratory data gradually worsened on account of pulmonary high flow. A cranial echocardiography on the second day after birth revealed bilateral subependymal hemorrhage with intraventricular perforation. The hydrocephalus gradually progressed after the 20th day of life. We considered that the infant would not be able to survive a radical heart surgery because of his low body weight, hydrocephalus and other characteristics. Continuous



**Figure 1** - Face of the patient. A: at birth, B: at 12 months old



CC; common chamber, CS; coronary sinus, LA; left atrium, LV; left ventricle, RA; right atrium, RV; right ventricle.

**Figure 2** - Echocardiogram at birth. A: four-chamber view, arrow indicates dilated coronary sinus, B: four-chamber view, blood flows into left atrium from right atrium

and persistent abdominal distension also made it difficult to get a favorable body weight gain. He underwent a ligation procedure of ductus arteriosus to decrease pulmonary high flow at seven months when his body weight exceeded 2,000 g (2,026 g). At that time, due to irreversible pulmonary hypertension, we were forced to abandon a radical operation on his heart. He underwent a ventriculoperitoneal shunt operation at eight months to reduce high intracranial pressure. The hydrocephalus improved at 10 months, as shown in the cranial ultrasound. He was successfully extubated at 11 months.

His physical and mental development was very poor. A spontaneous smile was seen at six months (four months corrected age). Head control appeared at about 12 months (10 months corrected age), but he could not turn over in bed at all. At one year old, his weight was 2,275 g (-7.2 SD) and his height was 48.1 cm (-11.1 SD). We tried to give him juice or formula milk orally in the dose of 5 ml since he was one year old and he could drink them well. We also began weaning just before the 13 month of life and he responded well, without vomiting.

Sudden cardiac arrest, attributed to pulmonary hypertension, occurred at 13 months and he underwent cardiopulmonary resuscitation and was reintubated. We were able to re-extubate two weeks later after the cardiac arrest episode. Consequently, he had paroxysmal ventricular tachycardia at 18 months and underwent cardiopulmonary resuscitation again. Regrettably, he died of cardiac failure at 19 months, his body weight was 2,340 g (-6.6 SD) and height 51.5 cm (-9.8 SD). We were not given permission to perform an autopsy.

## Discussion

The frequency of XYY males has been estimated to be 1:1,000 live births.<sup>1</sup> XYY males do not have any striking phenotypical abnormality; this frequency has been estimated from newborn surveys. The incidence of XYY syndrome is known to be slightly higher in European countries; 1:939<sup>2</sup> or 1:851,<sup>3</sup> than that in Japan; 1:1,780<sup>4</sup> or 1:1,522<sup>5</sup> live births. This chromosomal anomaly may involve a racial difference. However, the lack of information on the incidence of this syndrome in Brazil and in other South American countries prevents us from discussing its prevalence there.

XYY males are said to be relatively tall and have some behavioral problems, and their quod vitam prognosis is not poor.<sup>6</sup> Nonetheless, we have reported an XYY male infant with rather short stature and severe congenital heart disease. Cases with neurological and/or psychological problems<sup>(6)</sup>, urinary tract malformation,<sup>7</sup> hypogonadism<sup>8</sup> and so forth, have been reported before. Only one clinical case of XYY male with congenital heart disease (aortic stenosis and ventricular septal defect) has been previously reported.<sup>9</sup> Diego Nunez *et al.* reported a case with conduction disturbance and short stature.<sup>10</sup> However, there has been no case report of an XYY patient with congenital heart disease and short stature.

The cause of intrauterine growth retardation was not clear in this case. His mother was a heavy smoker and she had also smoked during pregnancy. However, his elder sister was born with normal body weight and health. The average birthweight of XYY males does not differ from that of normal controls.<sup>6</sup> Generally, patients with total anomalous pulmonary venous return (TAPVR) admitted to our hospital weigh approximately 2,800 g at full term delivery, which means that the birthweight of patients with TAPVR is

adequate for gestational age. Therefore, we cannot attribute his short stature to congenital heart disease alone. A radical heart surgery could not have been performed on account of his low body weight and intracranial hemorrhage, which occurred in the early neonatal period. Pulmonary hypertension is believed to have developed as a result of a relative high pulmonary flow. A palliative procedure was the only course of treatment. Another method of treatment was considered as well: adding a pulmonary artery banding when a ligation procedure of the ductus arteriosus was done, but we regarded that it might lead to severe right ventricular heart failure. However, the etiology of intracranial hemorrhage was not identified, and his unstable blood pressure may have been attributed to it. The diagnosis of TAPVR type IIa might have been that of cor triatriatum type IIA, but the clinical different diagnosis was rather difficult to determine. If the infant had been born with a birthweight greater than 2,000 g and intracranial hemorrhage had not occurred, we could have performed a radical operation and he might have been alive today.

Recently, Rauen *et al.* reported a patient with cardio-facio-cutaneous syndrome and 47,XYY,del(12)(q21.2q22) karyotype.<sup>11</sup> They reported that the patient had a small patent ductus arteriosus and a small foramen ovale and that the subsequent follow-up examinations were normal. Our patient had no apparent defect in chromosome 12q examined by a conventional chromosomal analysis, but we had no information on the possibility of a relation between the phenotype of our patient and the deletion in chromosome 12q, while our patient had been alive. We did not examine the chromosome in full detail.

We could find no previous article concerning XYY males with congenital heart disease. This combination of XYY male and congenital heart disease may be fortuitous. However, we think it is important to report that there was a poor prognosis case of XYY male with congenital heart disease and short stature.

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