CASE REPORT

Congenital extracardiac venous system anomaly in two siblings with normal karyotype and increased nuchal translucency thickness: a case report

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Abstract

Previous studies have reported that congenital heart diseases (CHDs) develop in patients with genetic and environmental predisposition. Compared to CHDs, the significance of hereditary factors in the pathogenesis of congenital venous system anomalies remains unclear. Additionally, reports describing the pathogenic relationship between venous system anomalies and increased nuchal translucency (NT) are few. We report sibling recurrence of congenital venous system anomalies. In the prenatal periods of both siblings, increased NT without aneuploidy was confirmed. In the first sibling, the absence of ductus venosus (ADV) and umbilical vein-coronary sinus anastomosis was detected using prenatal ultrasonography. In the second sibling, abnormality of the pulmonary vein was suspected prenatally, leading to a final diagnosis of infracardiac total anomalous pulmonary venous return (TAPVR). This is the first report of extracardiac venous anomaly-associated recurrence of increased NT among siblings. We conclude that a hereditary factor may be responsible for the development of ADV and TAPVR.

INTRODUCTION

Congenital heart diseases (CHDs) are known to develop in patients with genetic and environmental predisposition. Previous studies indicate that the recurrence rate is 2–5% among siblings with CHD; this is higher than that in the general population (1%) and suggests the relevance of genetic factors in the pathogenesis of CHD [1]. However, compared to CHDs, little is known about the hereditary factors, including their role in the pathogenesis of congenital venous system anomalies. Additionally, reports describing the pathogenic relationship between venous system anomalies and increased nuchal translucency (NT) are few. Hereby, we report a case of sibling recurrence of congenital venous system anomalies. This is the first documented case of increased NT associated with extracardiac venous system anomalies in two siblings.

CASE REPORT

A 32-year-old primiparous female was referred to our hospital, and an abnormal increased NT (6 mm) was found in the first trimester of the pregnancy. She had no complicated disease or history of hereditary disorders. Maternal risk factors, such as diabetes mellitus, obesity, smoking habit or alcohol consumption during pregnancy, were not reported. Chorionic villus sampling
Congenital extracardiac venous system anomaly in two siblings with normal karyotype

Figure 1: (Panel A) Longitudinal prenatal sonographic images of the fetus in the first pregnancy at 28 weeks. (Panel B) Color Doppler image of the fetus in the first pregnancy at 28 weeks. A connection between the umbilical vein and the inferior vena cava is lacking. An atypical vessel (arrow) is coursing from the portal vein (arrowhead) and flowing into the coronary sinus; RA, right atrium. (Panel C) Transverse prenatal sonographic images of the fetus in the second pregnancy at 32 weeks at the infracardiac level. (Panel D) The image of the fetus in the second pregnancy at 32 weeks at the infracardiac level. The pulmonary veins (arrowhead) join behind the left atrium, forming a common vertical descending vein (arrow); no direct connection between the pulmonary veins and the left atrium is visible; DA, descending aorta; LA, left atrium.

at 14 weeks of gestation demonstrated a normal karyotype. At 23 weeks of gestation, an abnormal dilated vessel was detected dorsally in the left atrium (Fig. 1, Panel A and B). After repeated sonographic examinations, agenesis of ductus venosus (ADV) and umbilical vein-coronary sinus anastomosis were diagnosed prenatally. The mother delivered a male neonate (weight, 3066 g; Apgar scores, 8/9; umbilical artery pH, 7.334) at 39 weeks. Except for extended hyperbilirubinemia, the postnatal course of the neonate was unremarkable without any circulatory problems, and he was discharged on day 7 after birth. Further, normal growth and development were observed until 6 years of age.

The same woman conceived again at 36 years of age. Increased NT (6.5 mm) was confirmed, similarly to that in her previous pregnancy. A normal karyotype was detected through amniocentesis. At 33 weeks of gestation, abnormality of the pulmonary veins was suspected under ultrasonography (Fig. 1, Panel C and D). The patient delivered a male baby (weight, 2480 g; Apgar scores, 8/8; umbilical artery pH, 7.305) at 38 weeks of gestation. An infracardiac total anomalous pulmonary venous return (TAPVR; type III: lower heart type) was eventually diagnosed in the neonate. Cardiac surgery was performed 15 days after birth with a successful postoperative course. Normal growth and development were confirmed until 3 years of age. No congenital anomalies were found in the history of the maternal or paternal families.

DISCUSSION

Previous studies showed that the incidence of ADV is 1 in 2500 singleton pregnancies [2], and TAPVR occurs in 1–3% of all cases of cardiac anomalies [3]. In previous reports on familial recurrence of TAPVR, chromosomal aberrations or gene abnormalities were identified as causative factors associated with disease development [4]. However, the significance of inherited factors in central venous system anomalies is not completely established. In this report, the siblings showed different types of venous anomalies, including ADV and infracardiac TAPVR type III. Therefore, based on these findings, we hypothesize that an unknown hereditary factor may be responsible for these venous anomalies.

In the early stages of fetal development (week 4–8), a complex pattern of vessel anastomosis and symmetric degeneration occurs in the umbilical vein (UV) and vitelline vein (VV) systems. A ductus venosus (DV) is formed following a connection between the left UV and the intrahepatic portion of the VV. Failure of this connection process results in ADV, which leads to abnormal shunting of the UV blood into the extrahepatic veins or the intrahepatic venous network. Nevertheless, in most cases with isolated ADV, the prognosis is good, as observed in the first sibling in this report [5, 6]. Pulmonary veins are formed at the same time as the pulmonary venous plexus during the fourth week of embryonic development. During the initial stage, the pulmonary venous plexus connects to common cardinal veins (CV), VV, and UV systems via the splanchnic plexus. During the fifth week, dorsal invagination of the left atrium is bound to the pulmonary plexus, and regression of the connection with other venous systems occurs. When this binding process between the pulmonary venous plexus and left atrium is impaired, connection to other venous systems continues, leading to the development of TAPVR [6, 7]. From an embryological standpoint, the onset of ADV and TAPVR occurs in a period similar to that of the development of the venous systems. Thus, it is possible that the ADV and TAPVR that developed in both the siblings resulted from a hereditary factor, which affects venous system formation, especially in the developmental stage.
Although past studies report an increased risk of CHD in chromosomally normal fetuses with increased NT [8], the association of extracardiac venous system anomalies with NT has not yet been established. The NT that was detected repeatedly in the two siblings implies that venous system anomalies can be considered a cause of increased NT. Furthermore, venous system anomalies may trigger an imbalance in the systemic fetal circulation in the early stages of gestation, leading to increased NT. In support of this hypothesis, studies have reported fetal hydrops caused by overperfusion of the liver sinusoids in a subgroup of ADV cases [9].

Although precise detection of isolated TAPVR in the fetus by ultrasonography is challenging, prenatal diagnosis of TAPVR contributes to improved postnatal outcomes [10]. In our cases, recurring findings of increased NT in both siblings, as well as the detection of ADV in the first sibling with normal karyotype, contributed to a prenatal diagnosis of TAPVR in the second sibling.

In conclusion, this report suggests that ultrasonographic scrutiny, which should include the extracardiac venous structure, is important in a fetus with increased NT.

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CONFLICT OF INTEREST STATEMENT
No conflicts of interest.

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ETHICAL APPROVAL
Not applicable.

CONSENT
Informed consent was obtained from the patient for publication of this case report and accompanying images.

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GUARANTOR
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