Pulmonary Stenosis in Recipient Twins in Twin-to-Twin Transfusion Syndrome: Report on 3 Cases and Review of Literature

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This report describes 3 cases of pulmonary stenosis in the recipient twin in twin-twin transfusion syndrome. Fetal echocardiography showed cardiomegaly, tricuspid valve regurgitation, and increased reverse flow in the inferior vena cava, as signs of congestive heart failure in all 3 cases. We diagnosed 2 cases of pulmonary stenosis by fetal echocardiography prenatally and confirmed our findings in all 3 cases postnatally. Two cases underwent postnatal balloon valvuloplasty to relieve the pulmonary valvular stenosis in neonatal period. The third one died soon after delivery and autopsy showed a slightly thickened pulmonary valve. One of the cases was diagnosed in the early second trimester (20 weeks of pregnancy), the earliest detection of fetal pulmonary stenosis reported in literature. The presence of high peak velocity of the pulmonary artery at 20 weeks of pregnancy preceded the development of pulmonary stenosis in this case. This supports the hypothesis that alterations in fetal hemodynamics may result in structural cardiac abnormality.

Key words: cross transfusion, intrauterine; fetal ultrasound; fetofetal transfusion; pulmonary stenosis; twin transfusion syndrome

Twin-twin transfusion syndrome is a severe complication in monochorionic twin pregnancies. A particularly severe complication in the twin-twin transfusion syndrome is fetal and neonatal cardiac dysfunction in the recipient twin followed by high perinatal morbidity and mortality (1-5). Although the pathophysiology of the syn drome is poorly understood, it is probably related to the presence of placental vascular anastomoses joining two fetal circulations (6). As a result of the circulatory disequilibrium, the donor twin becomes growth-restricted, oliguric, and develops oligohydramnios, whereas the recipient twin becomes polyuric, with severe polyhydramnios, and may develop hydrops. Most recipient twins develop cardiac dysfunction complicated with cardiomegaly, tricuspid and mitral valve regurgitation, ventricular hypertrophy, and increased reverse flow in the inferior vena cava (7-10).

Though a variety of cardiac complications has been reported, only a few cases of pulmonary stenosis in the recipient twins in twin-twin transfusion syndrome were described (7,11). In our report, we describe 3 cases of fetal and neonatal pulmonary stenosis in recipient twins in twin-twin transfusion syndrome. One of the cases is the first case that was diagnosed so early in the second trimester (20 weeks of gestation) and underwent postnatal balloon valvuloplasty to relieve pulmonary valvular stenosis.

Case Reports

Case 1

A 27-year-old primigravida was referred to our hospital at 26 weeks of gestation for acute polyhydramnios of one of the twins. A twin-twin transfusion syndrome was diagnosed according to the following criteria: inter-twin discordance in an estimated fetal weight with more than 20% difference, both fetuses of the same sex, disparity in size of the two amniotic sacs (poly- and oligohydramnios), and fetal hydrops of the recipient twin. Apart from cardiomegaly (52% of cardiothoracic area ratio), ascitic fluid, and pleural effusion in the hydroptic twin (recipient), ultrasound examination of the fetuses did not reveal any particular anomalies. Doppler study showed high preload
con ditions in the re cip i ent twin with a preload in-
dex of 0.76 and mas sive tricuspid and mi tral valve
re gur gi ta tions, whereas the umbilical artery and
descending aorta had normal flow velocity wave-
forms. To treat twin-twin transfu sion syn drome, a
massive am nio re duction was per formed on the
same day.

The next day, a ce sar ean de liv ery was done be-
cause the car diac dys func tion in the re cip i ent fe-
tus pro gressed and the tocolysis failed. Female
twins were de liv ered, the re cip i ent twin weigh ing
1,126 g and the don or twin 836 g. After their ad-
mis sion to the neo na tal in ten sive care unit, fur ther
examinations, in clud ing echocar diog raphy, re-
vealed cardiomegaly, mi tral valve re gur gi ta tion,
tricuspid valve re gur gi ta tion, ascites, and pleural
efu sion, as signs of a se vere con ges tive heart fail-
u re. When their con di tion sta bi lized, 9 days af-
ter birth echocar diog raphy was per formed show-
ing a pro longed ele va tion of right ven tri cul ar pres-
sure and a domed and thick ened pul mo nary valve.
Doppler echocar diog raphy re vealed a se vere pul-
mo nary val vu lar ste no sis and in creased peak sys-
tolic ve loc i ties of 4.6 m/s in the main pul mo nary
artery. The pul mo nary val vu lar ste no sis was re-
leased by per cuta neous bal loon val vu lo plasty. Af-
ter the di la ta tion of the pul mo nary valve, max i-
mum gra di ent be tween the pul mo nary ar tery and
right ven tri cle de creased from 48 mmHg to 13
mmHg, and gen eral con di tion of the baby im-
proved. How ever, two hours af ter the pro ce dure,
the baby fell into a shock caused by a mas sive pul-
mo nary bleed ing and died.

Case 2

A 27-year-old primigravida was re ferred to
our hos pi tal. She was preg nant with mono chlo-
ronic-di anmiotic twins, as de tected by ul tra sound
in the first tri mes ter.

At 18 weeks of ges ta tion, ul tra sound ex a mi-
na tion showed dis cor dant fe tal sizes and poly hy-
dramnios in the larger fe tus (re cip i ent). Doppler
studies of the in fe rior vena cava re vealed high
preload con di tion in the re cip i ent twin, with a
preload in dex of 0.88, whereas the preload in dex in
the do nor twin was nor mal (0.59). Both fe tuses had
nor mal wave forms in the um bli cal ar tery and vein.

At 20 weeks of ges ta tion, Doppler studies
showed an in crease in peak systolic ve loc i ty of the
re cip i ent’s main pul mo nary ar tery (1.72 m/s),
whereas the peak systolic ve loc i ty of the don or’s
was nor mal (0.57 m/s) (Fig. 1). Apart from ab nor-
mal ve loc i ties in the main pul mo nary ar tery and
ab normal preload in dex of the in fe rior vena
cava in the re cip i ent twin, close ultra sound ex a mi-
nation of the fe tuses did not re veal any par tic u lar
anomaly, such as struc tural heart anom aly or
cardiomegal y. Serial weekly ultra sound ex a mi-
nation, in clud ing color and pul sed Doppler, showed no
remarkable changes.

At 25 weeks of ges ta tion, the woman was
ad mitted to our hos pi tal for the treat ment of twin-
twin transfu sion syn drome, and serial am nio cen-
tesis was per formed. At 29 weeks of ges ta tion,
echocar diog raphy re vealed a slight cardiomegaly
and tricuspid valve re gur gi ta tion in the re cip i ent
fe tus, whereas find ings in the do nor fe tus were
nor mal. In this case, the main pul mo nary ar tery
peak ve loc i ties in the re cip i ent twin be came sig-
nif i cantly higher after 20 weeks of ges ta tion, in
con trast with a slight in crease in ve loc i ties of de-
scend ing aorta (Fig. 2).

A ce sar ean de liv ery was per formed at 30
weeks of ges ta tion be cause of un suc cess ful toco-
lysis and pro gres sion of the fe tal car diac dys func-
tion. Female twins were de liv ered, the re cip i ent
twin weigh ing 1,530 g and the do nor twin 882 g.
After ad mis sion to the neo na tal in ten sive care unit,
they un der went fur ther ex a mi na tions, in clud ing
echocar diog raphy, which de tected a car diac dys-
func tion, cardiomegaly, and tricuspid valve re gur-
gi ta tion in the re cip i ent twin. How ever, the peak
systolic ve loc i ty of the re cip i ent’s main pul mo nary
ar tery on the day of birth was nor mal. Sub se quent
echocar diog raphic ex a mi na tions re vealed that the
peak sys tolic ve loc i ties of the main pul mo nary ar-
tery in creased con se quently (1.6, 3.0, and 4.5 m/s

Figure 1. Doppler studies showing an in crease in the main pul mo nary ar tery peak sys tolic ve loc i ty (1.72 m/s) in the re-
cip i ent (A), and nor mal peak ve loc i ty (0.57 m/s) in the do nor (B) at 20 weeks of ges ta tion (Case 2).
at 15, 52, and 113 day, respectively), and also showed a pulmonary valve thickening and right ventricular hypertrophy.

Catheterization 135 days after birth showed a maximum gradient of 32 mmHg between the pulmonary artery and the right ventricle. The ratio between the right and the left ventricle pressure was 0.83. Subsequently, a balloon valvuloplasty was done to release pulmonary valvular stenosis. After the dilatation of the pulmonary valve, the maximum pressure gradient decreased to 20 mmHg, and general condition of the baby improved. She is now 4 years old and developing well.

Case 3

A 29-year-old woman, gravida 2 para 1, was referred to our hospital at 29 weeks of gestation for worsening of hydrops in the recipient twin in twin-twin transfusion syndrome. Ultrasound examination, including Doppler study, revealed cardiomegaly (38% of cardiothoracic area ratio), ascites, tricuspid valve regurgitation, a high preload in dext of the inferior vena cava (0.48), and increased peak systolic velocity of the main pulmonary artery (2.3 m/s) in the recipient twin. In the donor fetus, all findings on Doppler examination were normal.

Although amniocentesis was performed to treat the twin-twin transfusion syndrome, the recipient’s cardiac dysfunction progressed and twin-twin transfusion syndrome worsened. At 30 weeks of gestation, two female twin-babies were delivered by cesarean delivery. The birth weights of the recipient and the donor twin were 1,414 g and 824 g, respectively. The recipient twin died soon after the delivery because of severe congestive heart failure. We were unable to detect pulmonary stenosis in neonatal period, but autopsy showed slightly thickened pulmonary valve and biventricular hypertrophy.

Summaries of prenatal and postnatal echocardiographic findings are shown in Tables 1 and 2.

Discussion

In twin-twin transfusion syndrome, the main features of cardiac disease in recipient twin are cardiomegaly, tricuspid valve regurgitation, ventricular hypertrophy, and congestive heart failure. Although various cardiac diseases in recipient twins were reported, pulmonary stenosis in twin-twin transfusion syndrome is quite a rare condition. To our knowledge, only 5 cases have been previously described (7,11). Zosmer et al (7) reported 4 cases of pulmonary stenosis in recipient

Table 1. Prenatal and postnatal echocardiographic findings in recipient twins

<table>
<thead>
<tr>
<th>Case</th>
<th>Gestational weeks</th>
<th>Fetal weight</th>
<th>Prenatal&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Postnatal&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>UA-RI</td>
<td>CTAR (%)</td>
</tr>
<tr>
<td>1</td>
<td>26</td>
<td>1,126</td>
<td></td>
<td>0.76</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.83)</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>1,530</td>
<td></td>
<td>0.61</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.71)</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>1,414</td>
<td></td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.73)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data are presented as recipient (donor).

<sup>b</sup>Abbreviations: UA-RI—umbilical artery resistance index, CTAR—cardiothoracic area ratio, PLI—preload in dext of inferior vena cava, AAo—ascending aorta, DAo—descending aorta, PA—pulmonary artery, PS—pulmonary stenosis, TR—tricuspid valve regurgitation, MR—mitral valve regurgitation, ND—not detected.
Table 2. Postnatal findings in recipient twins

<table>
<thead>
<tr>
<th>Recipients</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>High velocity in pulmonary artery (4.6 m/s) and critical pulmonary stenosis, balloon dilatation on day 9 (48 to 13 mmHg). After the procedure, fell into shock caused by a massive pulmonary bleeding leading to neonatal death.</td>
</tr>
<tr>
<td>Case 2</td>
<td>Normal velocity in pulmonary artery on the day of birth, but peak velocity was increased consecutively, 2.1 m/s at 30 days, 3.0 m/s at 52 days, and 4.5 m/s at 133 days. Balloon dilatation on day 135 (32 to 20 mmHg).</td>
</tr>
<tr>
<td>Case 3</td>
<td>Pump failure on the day of birth leading to neonatal death. Post mortem examination showed slightly thickened pulmonary valve and biventricular hypertrophy.</td>
</tr>
</tbody>
</table>

- Change of maximum gradient between the pulmonary artery and the right ventricle.

Twins in twin-twin transfusion syndrome. One of these 4 cases was prenatally diagnosed with very high velocity (4.5 m/s) of pul monary artery. In that particular case, postnatal findings showed a critical pulmonary stenosis, and balloon dilatation of the pulmonary valve was done on the second day after birth. Other 3 cases were diagnosed postnatally and needed no balloon dilatation of the pulmonary valve. One case reported by Popeck et al (11) was diagnosed after the autopsy, which revealed pulmonary valve calcification.

In our report, we describe 3 cases of twin-twin transfusion syndrome with no signs of pulmonary stenosis in recipient twins. Two of them underwent balloon valvuloplasty and neonatal echocardiography, which revealed domed and thickened pulmonary valve but with out calcification. The third case also had a thickened pulmonary valve, as the autopsy revealed, and again no calcification was found.

Zosmer et al (7) reported a case of twin-twin transfusion syndrome with no signs of pulmonary stenosis in recipient twin's prenatal and early postnatal period. However, 4 months after birth, echocardiography showed a severe supravalvar pulmonary stenosis. Further more, our Case 2 had also a high peak velocity of the pulmonary artery in the prenatal period, whereas on the day of birth, the velocity was normal. Subsequently, the peak pulmonary artery velocity increased consecutively, but then infundibular stenosis was also revealed. According to these findings, we speculate that pulmonary stenosis in the recipient twin might be a progressive disease. Additionally, these findings support the hypothesis that alterations in fetal hemodynamics may result in structural cardiac abnormality, as reported by Hecher et al (12).

The etiology of pulmonary stenosis has not been fully clarified. Zosmer et al (7) speculated that pulmonary stenosis might be due to an increased afterload in the recipient twin because all of their cases had complicated tricuspid valve regurgitation. They also documented that the mechanism of recipient cardiac dysfunction, including pul monary steno sis, might be due to the increased afterload. High resistance to umbilical arterial flow in the monochorionic placenta could lead to increased afterload, in increased pressure in the systemic circulation of the recipient twin, high pressure in the ductus arteriosus, and obstructed outflow to the right ventricle, resulting in the development of congestive heart failure, right ventricular hypertrophy, and pulmonary stenosis. However, not all of the recipient twins who had hydrops and congestive heart failure had a right obstructive outflow tract and pul monary steno sis. Also, in the early stage of twin-twin transfusion syndrome, umbilical arterial vascular resistance is higher in the donor than in the recipient twin, because umbilical artery resistance/pulsatility index is higher in the donor twin. This fact suggests that in creasing afterload is not a direct cause of congestive heart failure in the recipient twin.

Most recipient twins in severe cases of twin-twin transfusion syndrome have complicated cardiomegaly, tricuspid valve regurgitation, and increased reverse flow in the inferior vena cava. These findings support the idea that congestive heart failure and hydrops fetalis in the recipient twins might originate from a chronic volume and pressure overload of the right ventricle. This chronic hyper-preload condition and pressure and/or volume overload lead to right cardiomyopathy and result in cardiomegaly and tricuspid valve regurgitation. However, all severely affected recipient twins did not necessarily have an asso ciated pul monary steno sis. It seems likely that some other feature is needed for pulmonary stenosis to develop and progress. In the neonatal period of the recipient twin in Case 2, infundibular pulmonary stenosis was found in addition to the pulmonary valve steno sis. On the basis of this finding, we may presume that pressure and/or volume overload to the right ventricle lead to a ventricle hypertrophy and/or right outflow tract obstruction.

It is difficult to say what is the main cause of development and progression of pulmonary stenosis. However, Case 2 is, to the best of our knowledge, the first case of pulmonary stenosis complicated by severe twin-twin transfusion syndrome that was followed up from the early second trimester. What was interesting in that case was that high increase in the peak velocity of the pul monary artery preceded such typical cardiac complications as cardiomegaly, tricuspid valve regurgitation, and increased reverse flow of the inferior vena cava. The other two cases were not followed up from early gestation because they were referred to our hospital at late second trimester, when hydrops and cardi dysfunction were in advanced stage.

Further more, it was difficult to assess when did the pulmonary stenosis in twin-twin transfusion syndrome appear and whether it appeared before the other cardiac complications or not. More studies focused on pulmonary stenosis are needed to understand the etiology of fetal and neonatal cardiac dysfunction and complications.
in the recipient twin in twin-twin transfusion syndrome.

References


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