Diagnosis, characterization and outcome of congenitally corrected transposition of the great arteries in the fetus: a multicenter series of 30 cases

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KEYWORDS: congenital heart disease; corrected transposition of the great arteries; fetal echocardiography; fetus; outcome

ABSTRACT

Objective To describe the anatomy, associated anomalies and outcome of 30 cases of congenitally corrected transposition of the great arteries (ccTGA) detected prenatally.

Methods This was a retrospective observational study of the 30 cases of ccTGA confirmed at autopsy or postnatal echocardiography seen at one of three referral centers from 1994 to 2003. The following data were considered: gestational age at diagnosis, cardiac anatomy, associated cardiac and extracardiac anomalies and fetoneonatal outcome. All fetuses underwent fetal echocardiography and a detailed anomaly scan, with follow-up scans at 3–4-week intervals until delivery. The diagnosis was confirmed at autopsy or after delivery. Follow-up data were retrieved from the clinical files of the patients.

Results The mean gestational age at diagnosis was 25.5 weeks. Intracardiac defects associated with the ccTGA included a ventricular septal defect in 21 cases, pulmonary outflow obstruction in 12 cases, an abnormal tricuspid valve in 10 cases, ventricular hypoplasia in five cases and dextro/mesocardia in five cases. The karyotype was normal in all 24 newborns, and unknown in the cases which resulted in termination of pregnancy (n = 5) or intrauterine death (n = 1). There were associated extracardiac anomalies in four cases only. Three of the four cases of atrioventricular block (AV block) developed in the third trimester, while the fourth appeared after birth. There were nine deaths (five terminations, two perinatal deaths and two infant deaths). The remaining 21 (70%) newborns were alive at a median follow-up time of 32 months, 11 of them after various surgical procedures.

Conclusions Our data suggest that in fetuses with ccTGA the risk of chromosomal and extracardiac anomalies is low, in accordance with postnatal data. The spectrum of associated cardiac lesions is consistent with that reported in the pediatric literature. These data may be of use during prenatal counseling since no figures regarding survival and/or outcome of ccTGA in the fetus have been reported so far. Copyright © 2006 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

Congenitally corrected transposition of the great arteries (ccTGA) is characterized by atrioventricular and ventricular arterial discordance. It represents a rare cardiac defect, accounting for 1.1% of cases of major congenital heart disease (CHD), and has an incidence at birth of 0.02 per 1000 live births. Prenatal diagnosis of this lesion is feasible, though relatively few cases have been described due to its rarity; those that have been described were in the context mainly of large fetal series of CHD. In addition, the defect may be difficult to detect at routine screening because the atrioventricular discordance may be overlooked if other significant anomalies of the four-chamber view are absent. To the best of our knowledge, this is the first case series addressing directly the diagnosis and natural history of ccTGA in the fetus. We report a retrospective observational study conducted on a population of 30 fetuses diagnosed with ccTGA confirmed at...
diagnosed in the fetus. Our objective was to analyze the
caracteristics, associations and outcome of ccTGA when
diagnosed in the fetus.

METHODS

This was a retrospective observational analysis including
all fetuses (n = 30) with a final diagnosis of ccTGA seen
at one of three referral centers (Fetal Cardiology Unit,
University Federico II of Naples & Pediatric Cardiology,
2nd University of Naples (joint unit); Obstetrics and
Gynecology, Di Venere Hospital, Bari; IRCSS G.Gaslini,

All examinations were performed with high-resolution
ultrasound systems (Prosound 5500 Aloka, Tokyo,
Japan; Voluson 730 Expert, General Electrics, Zipf,
Austria; Toshiba Powervision 6000, Tokyo, Japan). All
fetuses underwent fetal echocardiography and a detailed
anomaly scan. At fetal echocardiography, a sequential
segmental anatomical analysis was performed carefully
and ccTGA was diagnosed if both the atrioventricular
and the ventriculoarterial connections were discordant.
In particular, in ccTGA the venae cavae drain into the
morpological right atrium, which is connected to
the morphological left ventricle by a mitral valve (Figure 1).
From the right-sided morphological left ventricle emerges
the pulmonary trunk, which is located posteriorly and to
the right of the ascending aorta. The great arteries show
a parallel course and lack of crossing. Conversely, the
left atrium, receiving the pulmonary veins, is connected to
the morphological right ventricle through a tricuspid
valve (Figure 1); from this ventricle arises the transposed
aorta.

Follow-up scans were performed at 3–4-week inter-
vals until delivery. Autopsies or clinical/surgical files were
available to confirm the diagnosis of ccTGA in all cases.
Follow-up data were retrieved from the clinical files of the
patients.

RESULTS

Diagnosis and associated anomalies

The mean gestational age at the time of diagnosis
was 25.5 (range, 21–38) weeks, with 13/30 (43%)
cases diagnosed at <24 weeks of gestation. Regarding
the indication for fetal echocardiography, suspicion of
CHD at routine ultrasound was the referral reason for
the overwhelming majority of cases (28/30), while the
remaining two cases were fortuitously detected by two
of the authors (D.P., P.V.) during routine ultrasound. In
particular, the specific concerns of the referring sonologist
were: suspicion of Ebstein’s/tricuspid anomaly (n = 7),
suspicion of ccTGA (n = 6), suspicion of ventricular
hypoplasia (n = 5), dextrocardia (n = 4), suspicion of
ventricular septal defect (n = 3), suspicion of aortic
coarctation (n = 2), and non-visualized four-chamber
view (n = 1). Only 4/30 cases (13.3%) did not have any
associated intracardiac anomaly, the other 26 showing

one or more associated defects (Table 1). The diagnostic
accuracy was adequate, with only two cases of associated
atrial septal defect overlooked in utero. Extracardiac
anomalies were present in 4/30 (13.3%) cases and
consisted of mild to moderate renal defects (two cases
of bilateral hydrenephrosis, one case of duplex kidney
with mild vesicoureteral reflux and one case of grade
II vesicoureteral reflux). The karyotype was normal in
24/30 cases and unknown in the cases which resulted in
termination of pregnancy (n = 5) or intrauterine death
(n = 1), although in these cases there was no external
feature suggestive of underlying chromosomal anomalies
(e.g. low-set ears, typical facies, rockerbottom feet)
reported at autopsy.

Natural history

A heart block requiring early neonatal pace-maker
implantation developed in three cases during the third
trimester (31–34 weeks of gestation) and in one case after
birth. Two cases of re-entry tachycardia were recorded
after birth. When present, ventricular hypoplasia, due
to tricuspid atresia and/or straddling, was already severe
at the time of diagnosis; no case showed late failure of
ventricular growth. None of the 30 fetuses developed
cardiac decompensation in utero.

Fetoneonatal outcome

Figure 2 summarizes the outcome of the study pop-
ulation. There were six cases of intrauterine demise:
five (16.6%) terminations of pregnancy (severe associ-
cated cardiac anomalies were present in three cases, and
grade II vesicoureteral reflux in one) and one (3.3%)
unexplained intrauterine death. Eleven of the 24 live
births underwent various surgical procedures including
pulmonary artery banding, cavopulmonary anastomosis,

<table>
<thead>
<tr>
<th>Type of defect</th>
<th>This series</th>
<th>Pediatric literature*&lt;sup&gt;*,†&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>None</td>
<td>13.3 (4)</td>
<td>9–16</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>70.0 (21)</td>
<td>70–84</td>
</tr>
<tr>
<td>Pulmonary obstruction</td>
<td>40.0 (12)</td>
<td>30–50</td>
</tr>
<tr>
<td>Tricuspid anomalies†</td>
<td>33.3 (10)</td>
<td>14–56</td>
</tr>
<tr>
<td>Ventricular hypoplasia</td>
<td>16.6 (5)</td>
<td>NA</td>
</tr>
<tr>
<td>Dextro/mesocardia</td>
<td>16.6 (5)</td>
<td>25</td>
</tr>
<tr>
<td>Complete AV block</td>
<td>13.3 (4)</td>
<td>12–33</td>
</tr>
<tr>
<td>Aortic arch anomalies</td>
<td>10.0 (3)</td>
<td>13</td>
</tr>
<tr>
<td>Re-entry tachycardia</td>
<td>6.7 (2)</td>
<td>5.8†</td>
</tr>
</tbody>
</table>

* There was more than one anomaly in 26 cases. † Dysplasia ±
Ebstein-like attachment ± straddling (6 cases), atresia (4 cases).
‡ Including Wolf-Parkinson-White syndrome and rhythm
disturbances other than complete block. AV, atrioventricular; NA,
not available.

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Figure 1 Major ultrasound features in congenitally corrected transposition of the great arteries. (a) In the apical four-chamber view, the left atrium (LA) is seen to connect via an abnormal Ebstein-like tricuspid valve (TV) to a morphological right ventricle, which is characterized by the moderator band (arrow); in addition, the apex of the heart is formed by the morphological left ventricle (mLV) positioned on the right side. (b) In the transverse four-chamber view, the discordant atrioventricular connection is confirmed. In addition, the different wall attachments of the papillary muscles of the tricuspid and mitral valves are visible: the papillary muscles of the right-sided mitral valve attach on the lateral wall (arrowhead) whereas those of the left-sided tricuspid valve attach on the apical part of the ventricle (arrow). (c) In the short-axis view, the inverted position of the two ventricles can be seen, with the morphological right ventricle (mRV) positioned posteriorly and the mLV anteriorly. (d) The evaluation of the outflows demonstrates the parallel course and lack of crossing of the great arteries. Note the bifurcation which identifies the vessel arising from the mLV as the pulmonary artery (Pa). Ao, ascending aorta; Lt, left; RA, right atrium; Rt, right.

discussion

Anatomy

In postnatal life, ccTGA is associated with additional heart defects in most cases, the isolated variant of ccTGA accounting for only 9–16% of all cases. Associated anomalies include, in decreasing order of frequency: ventricular septal defects, pulmonary stenosis/atresia, anomalies of the left-sided tricuspid valve (including dysplasia, Ebstein-like attachment, straddling, tricuspid
atresia), rhythm disturbances and dextrocardia. In Table 1, the incidence and type of associated cardiac lesions in our fetal series is compared with figures derived from the pediatric literature. Our data are in fair agreement with those reported postnatally in larger series\textsuperscript{5–8,9}; this is rather uncommon for fetal series, which are usually skewed towards cases with unfavorable anatomy that are more likely to be detected during routine mid-trimester screening\textsuperscript{10}. Furthermore, in this series the diagnostic characterization of fetuses with ccTGA was adequate, with all major associated anomalies detected prenatally.

However, despite the good diagnostic accuracy shown by echocardiography, the prenatal recognition of ccTGA poses significant diagnostic difficulties in the screening setting, especially if the defect is not associated with severe atrioventricular abnormalities. It is therefore useful to underline the importance of some abnormal features that are easy to spot in the four-chamber view and that may contribute to improving the detection rate of ccTGA. First, a hint which may facilitate recognition of the atrioventricular discordance is provided by the insertion of the papillary muscles; those of the tricuspid valve tend to attach distally and centrally within the morphological right ventricle, while those of the mitral valve attach to the side wall of the morphological left ventricle. It should be stressed that the insertion of the papillary muscles is best displayed in a transverse four-chamber view, because with such an approach the insonation angle is optimal (Figure 1b). Another finding that may lead to the diagnosis of ccTGA is dextrocardia; this position anomaly is present in up to 25% of ccTGA cases in postnatal life\textsuperscript{9} and was found in 16.6% of the cases in our series (5/30). This anomaly is relatively easy to detect at screening ultrasound and usually leads to the suspicion of congenital diaphragmatic hernia or cardiopulmonary syndromes. However, according to our data, ccTGA should be included in the differential diagnosis whenever an apparently isolated dextrocardia is disclosed in a fetus. The third feature possibly leading to the diagnosis of ccTGA is the abnormal position and anatomy of the tricuspid valve (Figure 1). In the normal heart, the tricuspid septal leaflet is attached just below the insertion level of the mitral septal leaflet; in ccTGA, the lower leaflet is not on the right but on the left side of the heart and it is also frequently abnormal. The incidence of dysplasia of the tricuspid leaflets, which may or may not have been associated with a lower-than-normal insertion (Ebstein-like), was 20% both in our series (6/30; Table 1) and in postnatal ones\textsuperscript{9}. If the outflows are evaluated, the parallel course and lack of crossing of the great arteries represent the key features which may lead to the diagnosis.

Associated extracardiac anomalies and karyotype

Our data confirm that in the fetus ccTGA is rarely associated with chromosomal aberrations: all 24 liveborns had a normal karyotype and no external features suggestive of aneuploidy were reported at autopsy in the remaining six. This finding is worth emphasizing, since most CHD fetal series tend to report significantly higher aneuploidy rates than do pediatric ones\textsuperscript{5,6}. Likewise, in our experience the risk of association with extracardiac anomalies was negligible; there were only four such cases and all involved the kidney.

Natural history and evolution

So far there are scant data available regarding the perinatal course of ccTGA\textsuperscript{11,12}. In our series, there were four cases of complete atrioventricular block (AV block), three of which appeared in the third trimester, between the 31st and the 34th weeks of gestation. The remaining case of AV block and two cases of re-entry tachycardia were detected after birth. To our knowledge, this is the third time that prenatal onset of an AV block associated with ccTGA has been described\textsuperscript{11,12}. In addition, all cases born with severe ventricular hypoplasia presented with it at the time of diagnosis; in no case did we observe late reduction of ventricular volumes regardless of the degree of valve insufficiency and/or dysplasia.

Outcome and survival

The overall and adjusted (excluding terminations of pregnancy and intrauterine deaths) survival rates were 70% and 87.5%, respectively, at a median follow-up time of 32 months (Figure 1). These figures have limited use in postnatal counseling, due to the relatively short period of
follow-up. Nonetheless, since there are few data available regarding the prenatal course of ccTGA, they may be employed advantageously during prenatal counseling of parents of an affected fetus, to provide them with some figures regarding the short-term prognosis.

In conclusion, we have reported our experience with the diagnosis, characterization and outcome of fetuses with ccTGA. Although this observational study certainly has the significant drawback of including a relatively small number of cases, it represents, to the best of our knowledge, the first attempt at outlining the perinatal course of this uncommon type of CHD.

REFERENCES