Case Histories of Neonates with Congenital Heart Disease

MASUYOSHI NAGANUMA, M.D., MINORU TSUNEMOTO, M.D.*
AND TATSUO NAITO, M.D.**

The rate of extracardiac malformation (ECM) associated with congenital heart disease (CHD) is high in neonates. 108 cases of 212 neonates with CHD had ECM (50.9%). Main ECMs were digestive system anomalies (36.1%), chromosomal aberrations (26.8%), respiratory system anomalies (21.3%), CNS anomalies (13.0%), and others (2.7%).

Single lesion of left to right shunt accounted for 77.2% (61/79) of CHD with ECM from other than chromosomal aberrations.

The prognosis of neonates with CHD without ECM was also studied. Total anomalous pulmonary venous connection, pure pulmonary atresia (PPA), pulmonary stenosis (PS), hypoplastic left heart syndrome are not generally associated with ECM, but the prognosis is poor. Coarctation complex which is sometimes associated with ECM has a poor prognosis in neonates.

There is an increase of the survival rate in the patients with hypoxemia, such as PPA or severe PS, extreme tetralogy of Fallot, and tricuspid atresia, which can be managed with prostaglandin E1. PDA associated with respiratory distress syndrome is ideally treated with indomethacin. In recent years, mortality from PDA has decreased in neonates.

The mortality rate during the neonatal period was 46.8% (51/109): 37.5% (30/80) died before surgical interventions and 72.4% (21/29) died during or after surgery.

Half of neonatal deaths from CHD occurred within 3 days of admission. Thus, early detection, early diagnosis, and early treatment of neonates with CHD is most important.

NEONATES with congenital heart disease (CHD) are some of the most difficult patients to manage. In recent years, along with progress in diagnosis by non-invasive methods and in surgical techniques, active therapy for neonates with CHD has become possible. However, complications from surgical procedures are frequent and the death rate is high. In addition, the incidence of extracardiac malformations (ECMs) associated with CHD is high in neonates, requiring the cardiologist to manage the patients with their entire clinical picture in mind.

This study was undertaken to better determine the future direction in caring for neonates with CHD by analyzing the natural history and post-operative history of neonates with CHD.

SUBJECTS AND METHODS

1650 patients were autopsied in the National Children's Hospital of Tokyo for a period of 13
years from 1965 to 1978. 528 of these cases were neonates from 0 to 28 days of age. 212 of these cases (40.2%) had CHD and 108 (50.9%) had ECMs as well. There were 42 males and 66 females with a female to male ratio of 63.6%.

The prognosis for neonates with CHD without ECMs was studied in 109 cases. The subjects were patients from 0 to 28 days of age admitted to the division of neonatology for congestive heart failure or hypoxemia for a period of 5 years from 1973 to 1978.

RESULTS

The incidence of ECMs with CHD in neonates was high (50.9%). The types of ECMs associated with CHD are listed in Table I. Chromosomal aberrations were seen in 29 cases and accounted for 26.8% of ECMs (29/108). Respiratory system anomalies accounted for 21.3% (23/108), digestive system anomalies 36.1% (39/108), central nervous system (CNS) anomalies 13.0% (14/108), and others 2.7% (3/108). Chromosomal aberrations included 12 cases of Down’s syndrome, 12 cases of 18 trisomy syndrome, 3 cases of D1 trisomy syndrome, one of the 4P- syndrome and one of Turner syndrome. The main respiratory anomalies were hyaline membrane disease (12 cases), massive aspiration syndrome (6 cases), pneumothorax, and atresia of the bronchi. The main digestive anomalies were atresia ani (9 cases), esophageal atresia and/or trachea-esophageal fistula (13 cases), omphalocele (7 cases), duodenal stenosis or atresia (3 cases), Hirschsprung disease (one case), kidney anomalies (2 cases), and hypoplasia of the diaphragm (one case). CNS anomalies included intracranial or subarachnoidal bleeding (8 cases), meningocoele (2 cases), meningitis (2 cases), hydrocephalus (one case), and microphthalmos (one case). Other anomalies were congenital leukemia and Rubinstein-Taybi syndrome.

Chromosomal aberrations associated with ECMs (without CHD) occurred in 13 cases (10 with Down’s syndrome and three with 18 trisomy syndrome). All cases except one, had digestive system anomalies as well. The main digestive anomalies were atresia ani (4 cases), omphalocele (3 cases), duodenal stenosis (3 cases), and Hirschsprung’s disease (2 cases).

CHD with ECMs from other than chromosomal aberrations were PDA (28/79 = 35.4%), ASD (10/79 = 12.6%), VSD (6/79 = 7.6%), double shunts (14/79 = 17.7%), and triple shunts (3/79 = 3.8%).

Single lesions of the left to right shunt accounted for 77.2% (61/79) of CHD with ECMs. Most cases of ECMs with chromosomal aberrations were Down’s syndrome and almost all were associated with digestive anomalies.

CHD may be a fatal factor for neonates with ECMs. However, the lesions of CHD are almost

always simple, so active treatment is desirable. ECMs may also be fatal for neonates with CHD. However, in general, the prognosis of CHD does not take into account CHD with ECMs.

We also studied the prognosis of neonates with CHD without ECMs. The relation of neonatal severe CHD and mortality rate is seen in Figure 1, and the age at death from CHD in autopsied neonates is listed in Table II. It is known that total anomalous pulmonary venous connection (TAPVC), complete transposition of the great arteries (TGA), and pure pulmonic atresia (PPA) are not generally associated with ECMs, but the prognosis is poor. The prognosis of TGA improved due to balloon atrioseptostomy (BAS) but the survival rate for cardiac

Severe Neonatal CHD
from 1973 to 1978

TABLE III  SURVIVAL IN EACH PERIOD

<table>
<thead>
<tr>
<th>Condition</th>
<th>Admission</th>
<th>Neonatal period</th>
<th>Infancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGA</td>
<td>21</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>PA or severe PS</td>
<td>16</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>VSD &amp; PDA, ASD</td>
<td>12</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>TAPVC</td>
<td>11</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Coarctation complex</td>
<td>7</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Tricuspid atresia</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>PDA (isolated)</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Hypoplastic left heart</td>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>4</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>ECD</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ebstein anomaly</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Asplenia syndrome</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Interruption</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>11</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>109</strong></td>
<td><strong>58</strong></td>
<td><strong>39</strong></td>
</tr>
<tr>
<td><strong>(100)</strong></td>
<td><strong>(53.2)</strong></td>
<td><strong>(35.8)</strong></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 2. Clinical outcome of neonate cardiac anomalies.

surgery for TAPVC and pure pulmonic atresia (PPA) is poor. Other lesions with a bad prognosis during the neonatal period are coarctation complex, interruption of the aorta and hypoplastic left heart syndrome. The lesions of hypoxemia, such as extreme tetralogy of Fallot and pulmonary stenosis with tricuspid atresia, can be managed with prostaglandin E₁ before surgical treatment is attempted. This increased the survival rate after surgery. Thus, lesions with a relatively better prognosis within the neonatal period are tetralogy of Fallot, ventricular septal defect (VSD), TGA, and PDA. PDA associated with respiratory distress syndrome (RDS) is first treated with indomethacin, but if the medication has no effect, PDA is surgically ligated.

Clinical course of neonate cardiac anomalies is shown in Figure 2 and survival in each period is listed in Table III.

The mortality rate during the neonatal period was 46.8% (51/109). 37.5% (30/80) died before surgical intervention and 72.4% (21/29) died during or after surgery. The prognosis for CHD during infancy was also poor. The mortality rate

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of these cases during infancy was 27.5% (16/58). The mortality rate of those without surgical correction was 24.1% (7/29), and surgical mortality was 31.0% (9/29). Finally, the rate of neonates who reach infancy was only 35.8%.

The period of follow up from admission to death of neonates with CHD is shown in Figure 3. All except one died within 2 weeks. Half of them (27/51 = 52.9%) died within 3 days. Cardiac surgery was done in 21 cases within 9 days of admission. The type of cardiac surgery and survival rate are shown in Figure 4. Surgical procedures were almost always done within 2 weeks.

**DISCUSSION**

The rate of severe neonatal CHD was 3.6% (109/3000) of the out-patients in the cardiovascular division. Although the incidence of neonatal CHD is small compared with all CHD, knowledge of the natural course of the disease is most important for providing better management.

The incidence of ECMs with neonatal CHD was high (50.9%) compared with other ages! The incidence of ECMs decreased with age (Figure 5). The rate of ECMs was 27.5% in patients over one year and 13.6% in patients over 5 years of age?

The reason the incidence of CHD cases with ECMs is high is that CHD is one of the major anomalies in malformation syndromes. Treatment for ECMs as well as CHD must be done sufficiently during the neonatal period. As CHD as-
associated with ECMs may often be just a simple lesion of left to right shunts, active treatment for both CHD and ECMs should be undertaken.

The incidence of chromosomal aberration with cardiac anomalies was 13.6% (29/212) in the autopsied neonates with CHD. The over all incidence of chromosomal aberration with cardiac anomalies was 3.2% in the out-patient section of the cardiovascular division and 10.5% in the autopsy cases with cardiac anomalies\(^3\).

The incidence of chromosomal aberration with cardiac anomalies decreased with age and had a very poor prognosis. It was difficult to treat both CHD and ECMs in cases with chromosomal aberration and CHD.

The natural course of CHD associated with ECMs in neonates was different depending on the severity of ECMs. We also studied the course of CHD in neonates without ECMs. The prognosis of neonates with severe CHD is shown in Figure 2. Half of the neonates with CHD died either naturally or due to surgical procedures. Almost a third survived to one year of age. In theory, almost all CHDs except hypoplastic left heart syndrome are curable by surgical procedures, and active surgical treatment is needed, but the results of surgery at present are poor. Medical treatment by means of BAS, prostaglandin E\(_1\), and indomethacin is also important.

Half of the neonates with CHD died within 3 days of admission. Thus, early detection, early diagnosis, and early treatment of neonates with CHD is most important. Progress in non-invasive methods of diagnosis, surgical procedures, and the establishment of NICUs should also improve the rate of survival in the future.

REFERENCES