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Associated anomalies in congenital heart disease

Shimon Degani

The overall survival rate in infants affected by congenital heart disease remains low, ranging from 17 to 24%.[1–3] The poor outcome may be related to the increased association with extracardiac anomalies and aneuploidy.[4–7] Congenital heart defects have been considered to be the most common congenital anomaly encountered in liveborn infants.[8–10] The incidence has been estimated as five times higher in abortuses and stillbirths.[10–13] Noncardiac malformations have been reported to occur in 25–50% of patients with congenital heart disease.[4,5] The combination of cardiac anomalies with other organ abnormalities appears in genetic syndromes and sequences, chromosomal syndromes and after exposure to environmental factors (teratogenic drugs, infections and systemic maternal diseases).

Table 34.1. Syndromes with monogenic inheritance featuring cardiac lesions with a variable degree of penetrance. Modified from reference 14

Syndrome	*Mode of transmission*
Holt–Oram	AD
Noonan	AD
Apert	AD
Ehlers–Danlos	AD
Leopard	AD
Marfan	AD
Osteogenesis imperfecta	AD
Treacher Collins	AD
Tuberous sclerosis	AD
Carpenter	AR
Ellis–Van Creveld	AR
Friedrich ataxia	AR
Glycogenosis IIa, III, IV	AR
Ivemark	AR
Laurence–Moon–Biedl	AR
Meckel–Gruber	AR
Mucolipidosis II, III	AR
Mucopolysaccharidosis III, IS, IV, VI	AR
Refsum	AR
Smith–Lemli–Opitz	AR
Thrombocytopenia–absent radius	AR
Mucopolysaccharidosis II	XLR
Duchenne and Dreifus muscular dystrophies	XLR

AR, autosomal recessive; AD, autosomal dominant; XLR, X-linked recessive.

Congenital heart disease is considered to be a multifactorial disorder from the combined effects of a genetic predisposition and environmental factors in over 90% of cases.[14] A monogenic inheritance accounts for about 1–2% of affected infants. This figure includes specific cardiac lesions transmitted as single gene disorders and cases of congenital heart disease occurring with a variable degree of penetrance in syndromes with monogenic inheritance (Table 34.1). A chromosomal abnormality, most commonly an autosomal trisomy, accounts for 4–5% of patients (Table 34.2). In utero detection of cardiac defect is associated with a higher prevalence of chromosomal abnormalities.[4,15,16] An abnormal karyotype is seen almost twice as frequently in cases with combined anomalies than in cases with isolated anomalies.[16] Isaksen et al[4] reported on 63% of cardiac lesions with ventricular septal defect, atrioventricular septal defect, hypoplastic left ventricle and the combination of atrial septal defect and ventricular septal defect that were associated with chromosomal aberration. The high prevalence in this study is probably related to the frequency of amniocentesis in cases with congenital heart defects. Among 67 cases of congenital heart defects, the most frequent extracardiac anomalies were found in the urinary tract (28%) and central nervous system (CNS; 23%).[4] Cases with the combination of congenital heart defects and CNS anomalies had a high degree of chromosomal aberrations. In 1–2% of patients, environmental factors alone are thought to account for the heart anomalies, usually in combination with other anomalies (Table 34.3).

Table 34.2. Chromosomal abnormalities and congenital heart disease (CHD). Modified from reference 14

Chromosomal abnormality	*Incidence of CHD (%)*	*Most common lesions*
Trisomy 21	50	VSD, AV canal, ASD, PDA
Trisomy 18	99+	VSD, PDA, PS
Trisomy 13	90	VSD, PDA, Dex
Trisomy 22	67	ASD, VSD, PDA
Partial trisomy 22 (cat-eye)	40	TAPVR, VSD, ASD
4p-	40	ASD, VSD, PDA
5p- (cri-du-chat)	20	VSD, PDA, ASD
Trisomy 8 (mosaic)	50	VSD, ASD, PDA
Trisomy 9 (mosaic)	50	VSD, COA, DORV
13q-	25	VSD
+ 14q-	50	PDA, ASD, TOF
18q-	50	VSD
XO Turner	35	COA, AS, ASD
XXXXY	14	PDA, ASD, ARCA

ARCA, anomalous right coronary artery; AS, aortic stenosis; ASD, atrial septal defect; AV canal, atrioventricular canal; COA, coarctation of aorta; Dex, dextroversion; DORV, double outlet right ventricle; PDA, patent ductus arteriosus; PS, pulmonary stenosis; TAPVR, total anomalous pulmonary venous return; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

Table 34.3. Environmental factors and congenital heart disease (CHD). Modified from reference 14

Environmental factor	*Frequency of CHD (%)*	*Most common lesions*
Maternal alcoholism	25–30	VSD, PDA, ASD
Drugs		
Amphetamines	?5–10	VSD, PDA, TGA
Hydantoin	2–3	PS, AS, COA, PDA
Trimethadione	15–30	TGA, TOF, HLHS
Lithium	10	Ebstein's anomaly, tricuspid atresia, ASD
Thalidomide	5–10	TOF, VSD, ASD, truncus arteriosus
Infections		
Rubella	35	Peripheral pulmonary stenosis, PS, PDA, VSD ASD
Maternal conditions		
Diabetes	3–5 (30–50)	TGA, VSD, COA (For cardiomegaly and cardiomyopathy)
Lupus erythematosus	?	Heartblock
Phenylketonuria	25–50	TOF, VSD, ASD

AS, aortic stenosis; ASD, atrial septal defect; COA, coarctation of aorta; HLHS, hypoplastic left heart syndrome; PDA, patent ductus arteriosus; PS, pulmonary stenosis; TOF, tetralogy of Fallot; TGA, transposition of the great arteries; VSD, ventricular septal defect.

It is generally more difficult to detect congenital heart defects than it is to detect CNS or urinary tract anomalies.[17,18] Therefore, conscientious and thorough fetal echocardiography is a prerequisite for correct diagnosis after the finding of extracardiac anomalies. In the first trimester of gestation, although the heart is more difficult to examine by ultrasound and at autopsy, there are some extracardiac signs suggesting cardiac abnormality. In recent years, measurement of nuchal translucency in the first trimester has drawn attention as a noninvasive screening method for chromosomal abnormalities. In chromosomally normal fetuses fetal nuchal translucency above the 95th centile for crown–rump length at 10–14 weeks of gestation is associated with cardiac defects[19,20] and a wide range of skeletal dysplasias and genetic syndromes.[21] Accelerated edema may result from heart block of the type associated with complex heart disease. Nuchal edema formation was reported in cases with first-trimester fetal bradycardia that resulted from such heart blocks.[22] Preliminary results[23] suggest that abnormal ductus venosus blood flow in these fetuses identifies those with an underlying major cardiac defect.

Genetic syndromes associated with major cardiac defects

1. Tuberous sclerosis
2. Smith–Lemli–Opitz syndrome
3. Noonan syndrome
4. Cardiosplenic syndrome
5. Ehlers–Danlos syndrome
6. Marfan syndrome
7. Ellis–Van Creveld syndrome
8. Holt–Oram syndrome
9. Scimitar syndrome
10. Shprintzen syndrome
11. Apert syndrome
12. LEOPARD syndrome
13. Carpenter syndrome
14. Thrombocytopenia–absent radius (TAR) syndrome
15. Meckel–Gruber syndrome
16. Fryns syndrome
17. CHARGE association
18. VATER association

Tuberous sclerosis

Tuberous sclerosis is a single gene autosomal-dominant disorder characterized by multiple hamartoma formation. It shows a wide variability of expression. Prenatal diagnosis by means of a DNA or biochemical marker is not yet possible. Hamartoma formation is most commonly found in the CNS, the renal system and the heart. It is estimated that 5–86% of cardiac rhabdomyomas are associated with tuberous sclerosis.[24] Cerebral lesions, particularly those involving the basal ganglia and periventricular region, are usually smaller and more difficult to detect than cardiac masses,[25] but intracranial signs such as secondary ventriculomegaly may be detected earlier.[26] Fibroangiomatous skin lesions and cystic bone changes are probably undetectable prenatally; renal angiomyolipomas are not yet reported on prenatal sonograms.

Even where the cardiac lesion is single, the most likely diagnosis of fetal cardiac tumor is rhabdomyoma, with associated tuberous sclerosis. However, the characteristic features of this latter condition may not become evident until some months after birth.[27] Up to 80% of the individuals with tuberous sclerosis will have seizures and mental retardation, which are the most serious long-term complications of this disease.[28]

The combination of ultrasound findings with a maternal history of tuberous sclerosis allows the patient and her family to make a more educated decision regarding termination of the pregnancy.[29]

Smith–Lemli–Opitz syndrome

This is an autosomal recessive condition with a birth prevalence of about one in 20 000. It is associated with high perinatal and infant mortality. The features include severe mental retardation, characteristic minor facial anomalies, cleft palate, polydactyly and syndactyly, cardiac defects and, in the male, ambiguous or female external genitalia and deficiency of the enzyme 7-dehydrocholesterol reductase.[30] The defect in cholesterol biosynthesis, confirmed by reduced levels of amniotic fluid cholesterol, has facilitated prenatal diagnosis. Increased nuchal translucency thickness was reported in cases diagnosed sonographically in the first trimester.[31] Limb and genital defects are sonographic hallmarks of the syndrome later in gestation.

Noonan syndrome

This is an autosomal dominant condition with wide variability in expression; about 50% of cases represent new mutations. The birth prevalence is about 1 in 2000. Noonan syndrome is characterized by lymphedema thought to be due to dysplasia of the lymphatic system, short and webbed neck, short stature, heart defects (most commonly pulmonary valve stenosis), shield chest, hypertelorism and low-set ears.[32] Mild mental retardation is present in about one-third of cases. This syndrome is phenotypically similar to Turner syndrome, but with a normal karyotype. Nuchal thickening may disappear or continue into the second trimester and can occasionally lead to full-blown hydrops and risk of intrauterine death.[33,34]

Cardiosplenic syndrome (asplenia/polysplenia syndrome, heterotaxy syndrome)

Heterotaxy syndromes represent a defect in the lateralization of normal body asymmetry. These syndromes involve bilateral left-sidedness (polysplenia) or bilateral right-sidedness (asplenia).

The cardiosplenic syndromes are usually sporadic and associated with severe cardiac abnormalities. Anomalous pulmonary venous return, bilateral superior vena cava, endocardial cushion defect, dextrocardia and azygous continuation of the interrupted inferior vena cava[35] may be found along with right-sided stomach and midline liver. In the asplenia syndrome, cardiac anomalies may be more severe.[36]

The prognosis depends upon the severity of the cardiac defects. The mortality rate is very high, with a 1-year survival rate of 50%; only 10% live to adolescence.

Ehlers–Danlos syndrome

Two inherited disorders of connective tissue have major cardiovascular complications: Marfan syndrome and Ehlers–Danlos type IV.

Ehlers–Danlos syndrome is a heterogeneous group of diseases in which connective tissue laxity is the main feature. This syndrome results from mutation in the COL3A1 gene, which encodes the polypeptide in type III collagen. Despite advances in the molecular genetics of these two disorders, there is no molecular diagnostic test for the syndromes based on the identification of gene mutation. Biochemical analysis of the amount of type III collagen produced by dermal fibroblasts has proven to be a powerful diagnostic test for Ehlers–Danlos syndrome type IV. Prenatal diagnosis is possible by biochemical analysis of chorionic villus biopsies.[37]

The typical clinical features associated with this syndrome include dislocation of the joints other than the

hip, muscular hypotonia, and hyperelasticity, fragility and a doughy texture of the skin.[38] Aortic root dilatation and aortic dissection are frequent cardiovascular findings.

Marfan syndrome

This is an autosomal dominant connective tissue disorder with wide variability of expression. This disorder is thought to result from mutations in the fibrillin gene[39] followed by altered fibrillin metabolism, and is characterized by long limbs, tall stature, pectus deformities, ocular abnormalities and congenital heart defects. Cardiac defects primarily involve the ascending aorta and aortic valves, and less commonly the pulmonary artery or descending aorta.[40]

Ellis–Van Creveld syndrome (chondroectodermal dysplasia)

This is an autosomal recessive skeletal dysplasia characterized by short extremities, polydactyly, narrow thumb with short ribs and heart abnormalities, most commonly atrial septal defects. Ultrasound prenatal diagnosis is based on the demonstration of skeletal abnormalities. Atrial septal defects are difficult to detect early in pregnancy. Of affected infants, 30–50% die in the neonatal period as a result of pulmonary complications. Survivors have normal intelligence but very short stature.[41,42]

Holt–Oram syndrome

This is an autosomal dominant syndrome with variable expression, characterized by abnormal upper extremities and heart defects.[43,44] Cardiac abnormalities are primarily atrial and ventricular septal defects, sometimes associated with arrhythmia. Upper limb abnormalities include humeral, ulnar and clavicular abnormalities, radial hypoplasia, phocomelia, syndactyly and absent thumbs.

The gene responsible for this disorder is located on the long arm of chromosome 12. Prenatal diagnosis can be established in families with an affected parent by second-trimester ultrasound examination.[45]

Scimitar syndrome

This rare abnormality of unknown etiology and heredity consists of dextroposition of the heart and situs solitus secondary to right pulmonary hypoplasia and anomalous pulmonary venous return, draining into the inferior vena cava.[46]

Shprintzen syndrome (velo-cardio-facial syndrome)

This is an autosomal dominant syndrome characterized by short stature, mild mental retardation, ear and hearing abnormalities, micrognathia, limb abnormalities and cardiac defects. The syndrome is caused by the interstitial deletion of chromosome 22q11.21–q11.23.[47] This defect is thought to be related to DiGeorge syndrome; occasional abnormalities include absent T-cell function and absent thymic tissue.

Apert syndrome (acrocephalosyndactyly)

This syndrome is clinically characterized by typical facies features, acrocephaly and craniosynostosis and symmetrical syndactyly of the digits.[48,49] Apert syndrome is inherited as an autosomal dominant trait, and is considered to be a result of mutation in the gene of fibroblast growth factor receptor 2.[50]

Common findings that may be detected by ultrasound are: nuchal translucency in the first trimester, high forehead and flat occiput and flat face, hypertelorism, agenesis of the corpus callosum, osseous syndactyly and broad thumb. Heart defects such as tetralogy of Fallot are occassional findings.

LEOPARD syndrome (multiple lentigines syndrome)

This is a rare inherited disorder with autosomal dominant transmission associated with a high prevalence of cardiac abnormalities. LEOPARD: L, lentigines; E, electrocardiographic conduction defects; O, ocular hypertelorism; P, pulmonary stenosis; A, abnormalities of genitalia; R, retardation of growth; d, deafness.

Most patients with LEOPARD syndrome seem to lead a relatively normal life, cardiomyopathy being the cause of death in a few.[51,52]

Carpenter syndrome (acrocephalosyndactyly type II)

This is an autosomal recessive syndrome characterized by acrocephaly, syndactyly and preaxial polydactyly of hands and feet. Heart abnormalities may be found in 50% of affected individuals (septal defects, tetralogy of Fallot and transposition of the great arteries).

Craniosynostosis results in brachycephaly and acrocephaly, flat face with depressed nasal bridge and low-set ears.[53,54]

Thrombocytopenia–absent radius (TAR) syndrome

This is an autosomal recessive syndrome characterized by radial aplasia and thrombocytopenia. The radius is absent with hypoplasia or absence of the ulna, an abnormal humerus and absent fibula in half of the cases.

Congenital heart defects, primarily tetralogy of Fallot and atrial septal defects, are occasional findings. The diagnosis of thrombocytopenia can be confirmed prenatally by umbilical blood sampling.[55,56]

Meckel–Gruber syndrome

This is a lethal, autosomal recessive syndrome characterized by posterior encephalocele, postaxial polydactyly and cystic kidneys. Other abnormalities detectable by ultrasound are microcephaly, Dandy–Walker abnormalities, Arnold–Chiari malformation, microphthalmia, micrognathia, cleft palate and heart defects.[57,58]

Fryns syndrome

This autosomal recessive syndrome, usually lethal, consists of abnormal facies (micrognathia, broad nasal bridge, cleft lip and palate), abnormal corneas, distal digital hypoplasia, diaphragmatic defects, renal cysts and occasionally cystic hygroma and heart defects, in particular ventriculoseptal defects.[59,60]

CHARGE association

The acronym CHARGE stands for C, coloboma of the iris; H, heart defect; A, choanal atresia; R, intrauterine growth restriction; G, genital; and E, ear abnormalities.

The spectrum of defects might be attributable to arrested development 35–45 days after conception. It is unknown whether this condition is inheritable.

Heart defects detectable by ultrasound are: tetralogy of Fallot, double outlet right ventricle, endocardial cushion defect and ventricular septal defect.

Reports of antenatal ultrasonographic findings in the CHARGE association include severe polyhydramnios, mild ventriculomegaly, Dandy–Walker variant, small phallus and scrotum and small stomach.[61]

VATER association

This stands for: V, vertebral defects; A, anal atresia; T, tracheoesophageal fistula with E, esophageal atresia; R, radial and renal dysplasia. Heart defects may be occasional findings.[62] The etiology and heredity pattern of this condition are unknown.

Extracardiac anomalies associated with high incidence of congenital cardiac anomalies

A careful, systematic search for cardiac anomalies is indicated whenever an extracardiac anomaly is identified. Some anomalies listed below deserve special attention, and thorough echocardiography is mandatory because of the frequent association with cardiac anomalies.

Head and neck

1. Hydrocephalus
2. Agenesis of the corpus callosum
3. Cleft lip and palate
4. Cystic hygroma

Chest

5. Lung sequestration
6. Congenital cystic adenomatoid malformation of the lung

Wall defects

7. Diaphragmatic hernia

8. Omphalocele
9. Cloacal extrophy

Abdominal/gastrointestinal tract

10. Esophageal atresia with/without tracheoesophageal fistula
11. Duodenal atresia
12. Hepatomegaly

Skeletal

13. Camptomelic dysplasia
14. Thrombocytopenia–absent radius

Genitourinary tract

15. Renal dysplasia
16. Multicystic kidney

Others

17. Single umbilical artery
18. Nonimmune hydrops
19. Twins

Hydrocephalus

Hydrocephalus, defined as increased intracranial content of cerebrospinal fluid (CSF), is one of the most common congenital anomalies with an incidence of 0.3–0.8 per 1000 births.[63] In the majority of cases congenital hydrocephalus is the consequence of an obstruction along the normal pathway of the CSF. Abnormal accumulation of CSF results in enlargement of the ventricular system. Obstruction at the level of the aqueduct of Sylvius is found in the majority of cases of congenital hydrocephalus. Communicating hydrocephalus is caused by an obstruction to CSF flow at the level of the ventricular system.

Associated extracranial anomalies have been reported in 20–63% of hydrocephalus cases.[64,65] Cardiac anomalies in these cases included ventricular septal defect and tetralogy of Fallot.

Hydrocephaly, which may be accompanied by Dandy–Walker malformation, may be associated with a ventricular septal defect.[65] Dandy–Walker syndrome is characterized by the association of posterior fossa cyst; defect in the cerebellar vermis, through which the cyst communicates with the fourth ventricle; and a variable degree of hydrocephalus.

Agenesis of the corpus callosum

Agenesis of the corpus callosum may be complete or partial. As a consequence, the two lateral ventricles are set apart with upward displacement of the third ventricle. The sonographic appearance of the defect may be very similar to that of uncomplicated hydrocephaly. Agenesis of the corpus callosum can occur in chromosomal anomalies and may be a part of Mendelian syndromes.[66]

The defect is frequently associated with other anomalies of the CNS and other systems, including the cardiovascular system.[67] Cardiac anomalies mainly include conotruncal malformations, e.g. tetralogy of Fallot or double outlet right ventricle.[68] An association with tuberous sclerosis, mucopolysaccharidosis and maternal rubella has been reported.

Cleft lip and palate

Facial clefting constitutes a spectrum of lateral clefting defects involving the upper lip and/or palate. It is the second most common congenital malformation, accounting for 13% of all anomalies.[69]

Associated anomalies are found in 50% of patients with isolated cleft lip and in only 13% of those with cleft lip and cleft palate.[70] The association with congenital heart disease is of particular importance, but no specific pattern has been identified.[71]

Cystic hygroma

Cystic hygroma is a malformation of the lymphatic system characterized by a single cyst or multiple cysts within nuchal soft tissuse. Cystic hygromas are frequently found in association with chromosomal aberrations (mainly Turner syndrome) and consequently with a wide variety of anomalies.[72] The most common cardiac lesions in Turner syndrome are coarctation of the aorta, aortic stenosis and atrioseptal defects. Autosomal trisomies are also frequently associated with cystic hygroma and cardiac anomalies, including ventricular and atrial septal defects, pulmonary stenosis and atrioventricular canal (Table 34.2).

Lung sequestration

Lung sequestration is a congenital malformation in which a mass of pulmonary parenchyma is separated from the normal lung. Two varieties have been described: the *extralobar* variety, which is the most common in newborn

infants, and is characterized by a separate visceral pleura covering the sequestered lung; and the *intralobar* variety, in which the sequestered lung and the normal lung share a common pleura.

Extrapulmonary anomalies occur in 10% of patients with intralobar lung sequestration.[73] Among other anomalies, congenital heart anomalies include tricuspid atresia, transposition of the great vessels and subvalvular aortic stenosis.

In the extralobar variety the incidence of extrapulmonary anomalies is higher, up to 59%, including diaphragmatic hernia in 50% of cases[73] and heart anomalies such as atrial and ventricular septal defects, congenital absence of the pericardium and truncus arteriosus.[74]

The anomalous blood supply to the sequestered lung can cause a left-to-right shunt, leading to transient ascites[75] or hydrops in the fetus or cardiac failure after birth.[76]

Congenital cystic adenomatoid malformation of the lung

Congenital cystic adenomatoid malformation of the lung (CCAML) is a rare hamartoma of the lung in which there is adenomatoid overgrowth of terminal bronchioles at the expense of saccular spaces.

Classification of CCAML into three subtypes was proposed according to the size of the cysts:[77] type I has large cysts; type II has multiple small cysts of less than 1.2 cm in diameter; and type III, in which the worst prognosis is seen, consists of a solid noncystic lesion producing mediastinal shift.

Associated anomalies are frequently present in type II. The cardiac anomalies reported in association with CCAML are truncus arteriosus and tetralogy of Fallot.[78] Non immune fetal hydrops can result from decreased venous return due to vascular compression by the pulmonary mass or decreased myocardial contractility.

Diaphragmatic hernia

Congenital diaphragmatic hernia is secondary to a diaphragmatic defect leading to protrusion of abdominal organs into the thoracic cavity. The congenital hernias are classified according to the location of the diaphragmatic defect: (1) Bochdaleck hernia (posterolateral defect); (2) Morgagni hernia (parasternal defect); (3) septum transversum defect (central); (4) hiatal hernia (large esophageal orifice); and (5) eventration (weak diaphragm).

Cardiovascular abnormalities have been found in 23% of newborn infants with congenital diaphragmatic hernia.[79] The most common cardiac anomalies were ventricular septal defect and tetralogy of Fallot. Less frequent anomalies include coarctation of the aorta, ectopia cordis, atrial septal defect, absence of the pericardium and tricuspid atresia. The incidence of extracardiac anomalies was higher in infants with cardiac anomalies compared to those without cardiac disease. Cardiac anomalies were also reported in association with diaphragmatic hernia as part of chromosomal abnormalities (trisomy 21 and trisomy 18).[79]

Associated malformations in the neonate with congenital diaphragmatic hernia is a major factor influencing outcome in this malformation.[80]

Omphalocele

Omphalocele is a ventral wall defect charcterized by herniation of the intra-abdominal contents into the base of the umbilical cord with a covering amnioperitoneal membrane.

The frequency of chromosomal aberrations (mainly trisomy 13 and trisomy 18) varies between 35 and 58%. Cardiac anomalies are found in up to 47% of fetuses with omphalocele.[81]

The association of five anomalies constitutes a rare thoracoabdominal eventration, the pentalogy of Cantrell: (1) midline supraumbilical abdominal defect; (2) defect of the lower sternum; (3) absence of the diaphragmatic pericardium; (4) deficiency of the anterior diaphragm; and (5) intracardiac abnormality or ectopia cordis.[82] The incidence of omphalocele or diaphragmatic defect was found to be more than 30% among fetuses with congenital heart diseases and extracardiac anomalies.[4]

Cloacal exstrophy

Cloacal exstrophy is a rare anomaly of the caudal fold of the abdominal wall caused by a defect in the formation of the urorectal septum. Associated anomalies are very frequent and include genitourinary, gastrointestinal and skeletal anomalies. Spina bifida and separation of the pubic bones are the most common related anomalies.

Cardiovascular anomalies occur in 16% of patients.[83]

Esophageal atresia with/without tracheoesophageal fistula

The common embryological origin of the trachea and esophagus is the reason for the frequent association of

anomalies of these organs. Esophageal atresia is frequently associated with a fistula between the gastrointestinal and respiratory tracts. The etiology of esophageal atresia is unknown; it occurs sporadically.

The incidence of congenital heart disease varies between 15 and 39%. The most common cardiac abnormalities are atrial and ventricular septal defects.[84]

Duodenal atresia

Atresia and stenosis at the level of the duodenum is the most common type of congenital bowel obstruction.[85] Failure of canalization of the primitive bowel results in atresia presenting as a web or stricture of the bowel.

Congenital heart disease occurs in 8–20% of patients. These mainly include endocardial cushion defects and ventricular septal defects.

Approximately one-third of cases of duodenal atresia are associated with trisomy 21, with a high incidence of congenital cardiac anomalies (Table 34.2).

Hepatomegaly

Hepatomegaly is frequently secondary to congestive heart failure. The enlarged liver may be one of the manifestations of nonimmune hydrops in severe cardiac anomalies.[86]

Camptomelic dysplasia

Camptomelic dysplasia is a syndrome of dwarfism characterized by bowing of the long bones. Hydrocephalus and congenital cardiac malformation are frequently associated with the syndrome. Associated heart anomalies are atrial and ventricular septal defects, tetralogy of Fallot and aortic stenosis.[87]

Thrombocytopenia–absent radius

See above (p. 00) for a description of this syndrome.

Renal dysplasia/aplasia

Bilateral renal dysplasia or aplasia (agenesis) can be an isolated finding or can be a part of a syndrome. Absence of functioning kidneys has been associated with cardiovascular malformations in 14% of patients.[88] These anomalies include tetralogy of Fallot, ventricular septal defect, hypoplastic left heart, coarctation of the aorta, dextrocardia, single ventricle, transposition of the great vessels, total anomalous pulmonary venous drainage and tricuspid atresia.

Multicystic kidney

Multicystic kidney disease or polycystic kidney disease type II (Potter type II) is a congenital cystic renal disorder. The kidneys are symmetrically enlarged with cystic lesions that are composed of dilated collecting tubules replacing the normal renal parenchyma.

Multicystic kidney disease may be associated with cardiovascular malformations.[89] The associations include autosomal recessive syndromes such as Noonan, Smith–Lemli–Opitz and Fryns syndrome (see above under genetic syndromes).

Single umbilical artery

Absence of an umbilical artery is found in 1% of all deliveries.

Cardiovascular abnormalities are frequently associated with single umbilical artery including ventricular septal defect, atrial septal defect, coarctations and valve anomalies. Even when the single umbilical artery is an apparently isolated sonographic finding, the likelihood that the neonate will prove to have structural anomalies is considerable.[90] In 7% of cases, associated structural anomalies were reported and the most common organ involved was the heart.[90]

Nonimmune hydrops

Cardiac problems are relatively common causes of nonimmune hydrops.[91] The association of structural cardiac anomalies and fetal hydrops usually has a poor prognosis.[92] Defects that are severe enough to cause intrauterine congestive heart failure are responsible for the poor outcome. These include atrioventricular canal defect, tetralogy of Fallot, aortic atresia, aortic arch interruption, tricuspid dysplasia and Ebstein's anomaly, pulmonary dysplasia, intrapericardial teratoma, cardiac rhabdomyoma, ventricular septal defects and endocardial fibroelastosis. Even intrauterine myocardial infarction has been reported in association with nonimmune hydrops.[93]

Twins

The prevalence of congenital anomalies in twin pregnancies is higher than in singleton pregnancies. Congenital heart disease is not unique to multiple pregnancies, but occurs more often. Some anomalies are unique to multiple conceptions such as conjoined twins (thoracopagus) and twin reversed arterial perfusion sequence.[94,95]

Summary

The diagnostic workup of a possible congenital condition in which cardiac anomalies are associated with other anomalies is bi-directional. Detection of any structural cardiac anomaly should be followed by a thorough sonographic examination to exclude a possible extracardiac anomaly. Diagnosis of any extracardiac structural abnormality is an indication for thorough fetal echocardiography. The above-listed associations and syndromes may serve as a guide for such a workup.

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