Thai Journal of Obstetrics and Gynaecology
December 1999, Vol. 11, pp. 199-207

SPECIAL ARTICLE

Congenital Malformations in Twins

Atiwut Kamudhamas MD.

Department of Obstetrics and Gynecology, Faculty of Medicine, Thammasat University, Klongluang, Pathumthani, 12120, Thailand

ABSTRACT

Congenital malformations in twins are found infrequently but not uncommon, its prevalence varies greatly between 0.2 to 18.3 percent. In comparison with singletons, it is found more common in twin than in singleton pregnancy, especially in like-sexed twins. Between monozygotic and dizygotic twins, monozygotic twins are found to increase in prevalence of major and multiple anomalies, but same prevalence for minor anomalies. Main categories are divided into malformations unique and not unique to multiple conception. The first one consists of conjoined twins which is resulted from incomplete separation of a single embryo and acardiac twins which is resulted from vascular interchange theory. Congenital malformations not unique to multiple conception consist of congenital heart disease, positional defects, neural tube defects, GI, KUB anomalies, and chromosome anomalies which are mostly more common in twins. Etiology is not clearly understood, but thought to be a part of twinning process itself, which propose that their etiologic hypotheses are not the same as those in singleton pregnancy. Diagnosis, management, and prognosis are also discussed.

Key words : congenital malformations, twins

Congenital malformations in twins are found infrequently and knowledge about them is not precisely understood. Therefore, some physicians may somewhat not realize with this problem because of these reasons. This article has reviewed from varying issues to summarize its understanding.

Prevalence

Prevalence of congenital malformations in twins vary greatly between studies, ranged from 0.2 to 18.3 percent.[1-5] This variation was due to she differences in study method, including range of anomalies studied, completeness of examination, demographic differences, and chance variation as the number of affected twins studied is rather small.

It is mostly found that prevalence of congenital malformations are more common in twin than in singleton pregnancy, ratio of prevalence rate at birth of anomalies in twins to rate in singleton varies from 1.1 to 3.5.[1-5] There are only few studies contrastly reported the above findings.[5,6]

Within the group of twins , like-sexed twins are found to increase in prevalence of congenital malformations , ratio of prevalence rate at birth of anomalies in twins of like sex to rate in twins of unlike sex varies from 1.1 to 6.6.[1-6] When zygosity has been determined, monozygotic twins are found to increase in prevalence of major and multiple anomalies which are likely to be the result of an insult in early embryonic life, but (defects which occur in later life in utero) there are no different in prevalence of the between both monozygotic and dizygotic twins.[7]

Classification

There is no definite classification for congenital malformations in twins. From reviewing, it is more practical to divide congenital malformations in twins into two categories.

1. Malformations unique to multiple conception

1.1 Conjoined twins

Conjoined twins refers to incomplete anatomic separation of some location bet-ween monozygotic twins causing connection somewhere between two fetuses.[1-9]

1.2 Acardiac twins

Acardiac twins refers to a complex malformation associated with monozygotic, monochorionic twins, in which one twin has a severe abnormality involving malformations of the head, neck, and upper body with absent or rudimentary nonfunctioning heart.[1-9] Acardiac twins may also be called acardiac monster, holoacardius, or chorioangiopagus parasiticus.[1,5,9]

1.3 Fetus-in-fetu

Fetus-in-fetu refers to monozygotic twins which one fetus or parts of a fetus lodges within another fetus, hypothesis is similar to that of an acardiac twins.[1,5]

2. Malformations not unique to multiple conception

2.1 Congenital heart disease, ie, endocardial cushion defect

2.2 Positional defects, ie, talipes, hip dislocation, skull asymmetry

2.3 Neural tube defects, ie, spina bifida, anencephaly, encephalocele

2.4 GI, KUB anomalies, ie, esophageal atresia, TE fistula, cloacal extrophy

2.5 Chromosome anomalies, ie, Turner , Down's, and Klinefelter syndrome

Etiologic hypotheses

Although no definite theory, there are hypotheses about congenital malformations in twins , consists of

1. A part of monozygotic twinning process

1.1. Incomplete separation

Conjoined twins are thought to be an incomplete separation of a single embryo after the formation of two embryonic discs, mostly after 13 days of conception.[7,8] The precise reason for this events has not been established.

1.2. Factors at early embryonic period

It is not clearly understood to explain this theory, but all early embryonic malformations and malformation complexes such as sirenomelia, holoprosencephaly, cloacal extrophy, anencephaly, congenital heart disease, Goldenhar syndrome, de Lange syndrome, and Rubinstein-Taybi syndrome are increased in monozygotic twins. The reason for this association is considered to be the common etiology for both the monozygotic twinning and the early malformation problem.[1,7,8,10] This category is supposed to be the result of interaction between two fetuses, maternal tissues might accept less easily to antigenically different and competing trophoblasts leads to an anomaly of one or two fetuses, neural tube defects is the most typical explanation in this theory and some investigators suggest that there are different in etiology between twin and singleton pregnancy for this group of anomalies.[11,12]

2. Vascular interchange

This etiology results from any vascular interchange between the monozygotic twins. This reason is explained for acardiac twins, amorphous twins, and fetus-in-fetu. Vascular connection between twins leading to reversal of blood flow to one twin, called the twin reversed arterial perfusion (TRAP) sequence, causing one "perfused" and the other "pump" twin. Perfused twin receives unoxygenated blood resulting in aplasia of the heart, head, and upper limbs. The pump twin is usually morphologically normal, or may sometimes have heart failure and hydrops.[1,4,5] This category may also include microcephaly, porencephalic cysts, hydranencephaly, intestinal atresia, aplasia cutis, and limb amputation.[7,8] This vascular interchange theory is exclusively observed in monocho-rionic, especially monoamniotic placentation in monozygotic twins. Monochorionic diamniotic placentation is less common, but also typical.[1,3,7] Dichorionic diamniotic monozygotic twins can be found as rare cases.[13] Moreover, it has also been reported in dizygotic twins

twins. Monochorionic diamniotic placentation is less common, but also typical.[1,3,7] Dichorionic diamniotic monozygotic twins can be found as rare cases.[13] Moreover, it has also been reported in dizygotic twins as a very rare case where the placenta has fused.[14,15]

3. Factors in utero during late gestation

This etiology explains for other malfor-mations that prevalence rate does not differ between monozygotic and dizygotic twins.[6,7] The examples in this category are cleft lip, cleft palate, and other minor anomalies.

4. Limited space

Some positional defects such as talipes, hip dislocation, and skull asymmetry are also more common in twin than in singleton pregnancy, this category is thought to be the consequence of limited growing space and relative restriction of movement, but this fact has not been proven.[7] This twins associated defects are usually resolved quickly and spontaneously, true talipes equinovarus and congenital hip dislocation are more likely from genetic factor.[5]

Noted some common malformations and their points of interest on prevalence and hypotheses are summarized in Table 1.

Diagnosis

1. Clinical examination

Clinical manifestations on the mother vary remarkably. It can be range from high degree of suspicion to normal twin uterus. Marked overdistended uterus is common due to polyhydramnios which can be occurred in acardiac twins, conjoined twins, NTD, and GI malformations. On Leopold's maneuver, some conjoined twins may be found that two fetal heads lie closely and move together to another lie in different time. Twins with discordant or concordant anencephaly may be found that global shaped fetal head is undetected while multiple small parts of the fetuses are palpable. On the other hand, some anomalies such as acardiac twins with just an amorphous mass may produce different clinical entity with small uterus and may mislead as a singleton pregnancy.

2. Maternal serum markers

As generally known, screening on maternal serum markers can assist to assess candidates for prenatal diagnosis, for examples, increased alpha-fetoprotein is found in neural tube defects and decreased alpha-fetoprotein in chromosome anomalies. In twins, serum markers have more diagnostic dilemma according to twins itself which may influence the effects of serum markers level. Upto dates, maternal serum markers in twins are under investigation as aspects of interests.[16,17]

3. Ultrasound

It is recommended that when even multiple gestation are suspected clinically, serial real time ultrasound scans should be obtained beginning in the first trimester,[18] and ultrasound has definitely proved of value in detection of anomalies in twins in the second trimester.[19] Ultrasound findings of conjoined and acardiac twins are shown in Table 2. Ultrasound findings of congenital malformations not unique to twins are alike those of singleton fetuses, so there are not mentioned here.

Table 1. Some common malformations and their prevalence and hypotheses[1-10,12-15,20-23]

	Hypotheses	Prevalence	Inherited pattern	Zygosity, Chorionicity	Sex ratio	Number of sharity
Conjoined Twins	Incomplete Separation of a single embryo after day 13th	1 : 50,000 to 1 : 100,000 births and 1:100 to 1:200 MZ twins	sporadic, and no recurrent risk	MZ only, MC-MA (MZ:monozygotic MC:monochorionic MA:monoamniotic)	like-sex only, F>M (F=75%) (F:female)	concordant
Acardiac Twins	Vascular Connection	1:30,000 to 1:35,000 births and 1:100 in MZ twins	sporadic	MZ a rule, MC a rule, MA>DA, MZ-DC rare, DZ very rare	like-sex a rule, unlike-sex rare, F/M vary	concordant
Congenital Heart disease	Disturbance in laterality of embryo's hemodyna-mic gradient	increase in twins compared with singleton	sporadic, increase recurrent If same environs	MZ>DZ (DZ:dizygotic DC:dichorionic DA:diamniotic)	like-sex> unlike-sex	discordant> concordant, concordant rate=6.8% only
Neural tube Defects (anencephaly encephalo-cele and spina bifida)	contact and interaction between two trophoblasts etiology is thought to be different from those in singletons	1.6:1,000 twin births(1:1,000 in singletons), increase in anencephaly and encepha-locele, but decrease in spina bifida	sporadic, recurrent risk = 8% if next pregnant is twins, and risk= 1-2% if singleton	MZ>DZ	like-sex> unlike-sex, F>M,(F= 55-80%) (F:female M:male)	discordant> concordant, concordant rate=3.7% only
GI,KUB (esophageal atresia,TE-fis-tular,cloacal extrophy)	Twinning reaction in early embryonic period	five-fold increase in twins compared with singleton	sporadic, recurrent rate is low	MZ>DZ	like-sex> unlike-sex	discordant> concordant, concordant rate=5% only
Positional Defects (talipes)	limit space, restriction of movement	increase in twins,but for mild defects	none	variable	variable	variable

twins. Monochorionic diamniotic placentation is less common, but also typical.[1,3,7] Dichorionic diamniotic monozygotic twins can be found as rare cases.[13] Moreover, it has also been reported in dizygotic twins as a very rare case where the placenta has fused.[14,15]

3. Factors in utero during late gestation

This etiology explains for other malfor-mations that prevalence rate does not differ between monozygotic and dizygotic twins.[6,7] The examples in this category are cleft lip, cleft palate, and other minor anomalies.

4. Limited space

Some positional defects such as talipes, hip dislocation, and skull asymmetry are also more common in twin than in singleton pregnancy, this category is thought to be the consequence of limited growing space and relative restriction of movement, but this fact has not been proven.[7] This twins associated defects are usually resolved quickly and spontaneously, true talipes equinovarus and congenital hip dislocation are more likely from genetic factor.[5]

Noted some common malformations and their points of interest on prevalence and hypotheses are summarized in Table 1.

Diagnosis

1. Clinical examination

Clinical manifestations on the mother vary remarkably. It can be range from high degree of suspicion to normal twin uterus. Marked overdistended uterus is common due to polyhydramnios which can be occurred in acardiac twins, conjoined twins, NTD, and GI malformations. On Leopold's maneuver, some conjoined twins may be found that two fetal heads lie closely and move together to another lie in different time. Twins with discordant or concordant anencephaly may be found that global shaped fetal head is undetected while multiple small parts of the fetuses are palpable. On the other hand, some anomalies such as acardiac twins with just an amorphous mass may produce different clinical entity with small uterus and may mislead as a singleton pregnancy.

2. Maternal serum markers

As generally known, screening on maternal serum markers can assist to assess candidates for prenatal diagnosis, for examples, increased alpha-fetoprotein is found in neural tube defects and decreased alpha-fetoprotein in chromosome anomalies. In twins, serum markers have more diagnostic dilemma according to twins itself which may influence the effects of serum markers level. Upto dates, maternal serum markers in twins are under investigation as aspects of interests.[16,17]

3. Ultrasound

It is recommended that when even multiple gestation are suspected clinically, serial real time ultrasound scans should be obtained beginning in the first trimester,[18] and ultrasound has definitely proved of value in detection of anomalies in twins in the second trimester.[19] Ultrasound findings of conjoined and acardiac twins are shown in Table 2. Ultrasound findings of congenital malformations not unique to twins are alike those of singleton fetuses, so there are not mentioned here.

Table 2. Ultrasound findings in conjoined and acardiac twins[1-5,9,21]

	Conjoined twins	Acardiac twins
Fetus	Two fetuses lie adjacent to each other and do not move apart with fetal movement. Joining part of the fetuses is visible, most common at the thorax as called thoracopagus. Other joining parts may exist at the head (craniopagus), inferior rump (ischiopagus), posterolateral rump (pygopagus), back above sacrum (rachipagus). Sometimes there may be two heads with one body (dice-phalus),or even two faces with one head and body (diprosopus).	There are two different fetus, one is the normal pump twin, the other is acardiac twin. The acardiac twin get its blood supply from pump twin, it either has no head or anencephaly. Its upper trunk and neck area will be thickened. An omphalocele may be present. Upper limbs are sometime absent. Club feet and absent toes are often seen. No cardiac pulsation. Limb movements are sometimes visible in acardiac fetus. The other twin, so called pump twin, are often normal. It sometimes may show sign of hydrops with hepatosplenomegaly, cardiomegaly, ascites, and pleural effusion.
Amniotic Fluid	Polyhydramnios is common. It can be found up to 75 percent of cases.	Polyhydramnios is common. If two sacs, polyhydramnios is found with pump twin and oligohydramnios with acardiac twin.
Membrane	No membrane	No membrane or sometimes thin membrane
Cord	Usually normal	Single umbilical artery is found 50% of cases
Placenta	Normal	May be enlarged with fetal hydrops
Time detectable	As early as 9 weeks	As early as 12 weeks

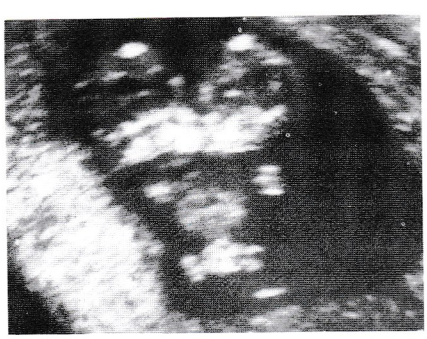

Fig. 1. Sonographic finding in conjoined twins, as early as 10 weeks by vaginal probe showing one body with two heads.[26]

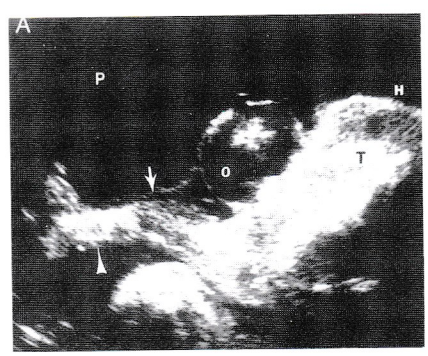

Fig. 2. Sonographic finding in acardiac twins, showing hydropic fetus without head, and also omphalocele.

4. Color Doppler velocimetry

Color Doppler may help to look in detail at fusion site of conjoined twins, for example, common liver arterial circulation or common cardiac systems. Its details can confirm diagnosis and suggest therapy after births.[21]

In acardiac twins, color Doppler may help to determine site of vascular connection, assess circulatory health of the normal fetus, and assess sign of heart failure or hydrops in the pump twin.[24,25]

In congenital malformations not unique to twins, color Doppler is helpful to assess fetal health status, and much helpful to confirm diagnosis in congenital heart defects.

5. Fetal echocardiography

Fetal echocardiography is exclusively helpful to establish diagnosis for congenital heart defects and plan the management.[27]

6. Chromosome study

Chromosome study is usually unneeded in conjoined twins, acardiac twins, and twins with neural tube defects. In twins with heart, GI, and KUB anomalies, chromosome study is usually required, it can be performed pre-natally by amniocentesis or cordocentesis.[28] When one anomaly has been detected, other anomalies must be looked for, and if there are multiple , chromosome study is required. [28] Some chromosome anomalies have more prevalence in twins than in singleton, such as 45,XO (Turner syndrome), 47,XXY (Klinefelter syndrome), therefore, when routine ultrasound scanning is performed, it must also be realized to look for detectable sonographic findings of those chromosome anomalies , for example, cystic hygroma, lymphangioedema, ascites, congenital heart disease, renal anomalies, and oligohydramnios can be observed in Turner syndrome, and if these findings are detected, chromosome study is required.[29]

7. Gross descriptions

Gross descriptions of the fetuses after birth or termination are definitive diagnosis for conjoined twins, acardiac twins, and twins with neural tube defects. For twins with congenital heart , GI, and KUB anomalies, further investigations including an autopsy may be required for definitive diagnosis.[5,9] Examples of grossly malformed neonates are shown in Figure 3 and 4.

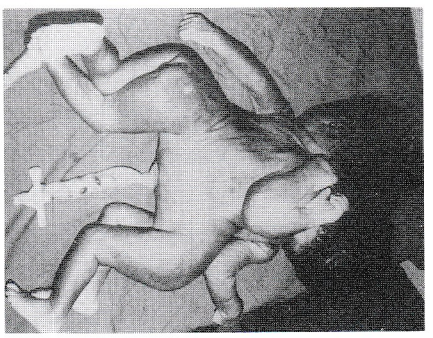

Fig. 3. Newborn with thoracopagus

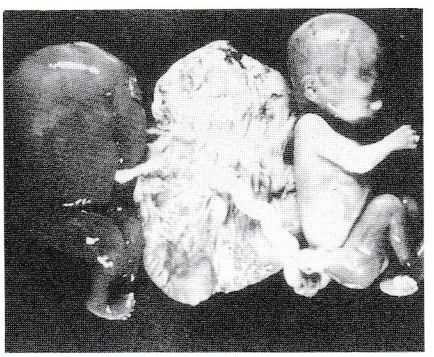

Fig. 4. Newborn with acardiac twins

Management

Antepartum, intrapartum, and postnatal management of conjoined twins and acardiac twins are discussed in Table 3.

anencephalic fetuses, the affected fetus is precisely not able to survive after birth. If twin pregnancy is concordant for anencephaly, management is simple by termination. But in

For congenital malformations not unique to multiple conception, management must be individually decised upon nature of disease, chorionicity of twins, compatibility to survive after birth, possibility of treatment, and prognosis. Decision must also follow parental discussion.[1,2] For example, in twins that have case of twins, which is much more common, discordant

Table 3. Management of conjoined twins and acardiac twins.[8,30-33]

	Antepartum	Intrapartum	Postnatal
Conjoined twins	1.Perform fetal echocardiography to assess cardiac structure, and serial ultrasound every 3-4 weeks to monitor growth and fetal demise. 2.Consult neonatologist and child surgeon to assess prognosis for separation and perinatal plan. 3.No fetal therapy is indicated, except releasing polyhydramnios.	1.Termination of pregnancy may be discussed with parents if early diagnosis is made 2.At delivery, well planned cesarean section in tertiary center is advised.	1.Respiratory support must be ready as early as first breath of life, as well as warmth, nutrition, and protection from infection. 2.Separation is varied on severity and timing must be discussed.
Acardiac twins	1.Serial ultrasound every 1-2 weeks to assess growth status, hydrops,or death of the pump twin. 2.Fetal therapy may be attempted, such as maternal digitalization, serial amniocentesis, maternal indomethacin therapy, endoscopic cord ligation, thrombosis of the umbilical artery by percutaneous thrombogenic coil or laser therapy, and hysterotomy with selective delivery of the perfused twin.	1.Conservation as long as possible until complications develop in the pump twin, then delivery is indi-cated, and should be performed in tertiary center. 2.Vaginal delivery is allowed unless fetal distress.	1.Respiratory support is essential, care must be emphasized on cardiac function as heart failure is commonly developed. 2.Prematurity is very common, care for RDS must be prepared. 3.Support parents for inevitable death of the perfused twin.

for anencephaly, chorionicity must be one of the determining factor. In monochorionic twins, expectant management is the only way unless the other fetus is unhealthy. In dichorionic twins, selective fetocide may be performed to prevent complications of twin pregnancy such as preterm labour, malpresentation, and iron deficiency anemia. It is also able to prevent polyhydramnios from anencephalic fetus that can superimpose complications of twin pregnancy, and can reduce cesarean section rate especially from twin associated indication but the parents can look after only one child. Amniocentesis to release polyhydramnios is another one of the management options. However, counseling with the parents is essential because each procedure has its risks. For example, selective fetocide in the second trimester-dichorionic twins proves to prevent the development of polyhydramnios and is associated with a lower risk of preterm delivery but can cause miscarriage upto the one-fifth of cases.[34] While there is some suggestion that expectant management may produce more favorable outcome for the unaffected fetus with no higher risk of miscarriage from a selective termination and has acceptable short and long term outcomes to the infants.[35] These options and risks must be discussed with the parents and treatment of other congenital malformations not unique to multiple conception should follow by this demonstration.

Prognosis

In conjoined twins, prognosis for survival depends on potential for separation of the connected infants which is related to the location of the union, the status of share vital organs, and the presence of associated organ malformations.[8] Well planned elective cesarean section in tertiary center also help to improve prognosis.[9] Timing for separation has effect on success rate and long term survival, the best result encounters when separation has been performed in the second and third month of life.[30]

In acardiac twins, all of the perfused twins die, while the pump twin has a 50 percent mortality rate.[9] The pump twins most commonly die from congestive heart failure, the rests are from prematurity.[36] It is found that the mean birthweight ratio in twins born before 34 weeks was up to 60 percent.[36] Well planned perinatal management in tertiary center by prenatally diagnostic ultrasound can help to improve prognosis.

In congenital malformations not unique to multiple conception other than positional defects, prognosis depends on severity of anomaly, associated anomalies, number of affected fetuses (concordant or discordant), and management policy.[4,5] For positional defects ; i.e. , talipes, skull asymmetry, and hip dislocation, all have excellent prognosis with mostly quick and spontaneous resolution and there is no recurrent risk.[5,6]

Discussion

Congenital malformations in twins are not uncommon. The malformations unique to multiple conception are special, obstetricians should have knowledge on them, especially to diagnose. Management should be obtained in tertiary center. In malformations not unique to multiple conception, it is exclusively striking to try to understand their hypotheses because their prevalent rates are increased in twins. As previously mentioned , there are explained by twinning process, vascular interchange, and so on. But finally, some investigators propose that may twins itself be a malformation process? More studies are needed.

Twins may be one of good models to study about congenital malformations and their clinical relevant. Examples, difference in FHR patterns between anencephalic and normal fetus were observed after week 28th in monozygotic twins with discordant anencephaly[37], and difference in fetal behavior observing in 2nd and 3rd trimester may indicate that the development of the CNS above the medulla oblongata plays an important role in fetal movement and fetal breathing movement.[38] Other instances, there are reports about malformations occurring from genetic disorder with same genotypic defects in twins which cleavage from the same zygote (monozygotic twins) but have different or variable phenotypic expression[39,40], it indicates that embryology is complicated with may sometimes not be able to be simply explained. Therefore, it is discussed that twins are one of good models for genetic and embryologic learning. Other studying and reports is really required.

References

1. Little J, Bryan E. Congenital anomalies in twins. Semin Perinatol 1986;10:50-2.
2. Layde PM, Erickson JD, Falek A, Mc Carthy BJ. Congenital malformations in twins. Am J Hum Genet 1980;32:69-78.
3. Myrianthopoulos NC. Congenital malfor-mations: the contribution of twin studies. Birth Defects 1978;14:151-65.
4. Hay S, Wehrung D. Congenital malfor-mations in twins. Am J Hum Genet 1980;22;662.
5. Bryan E. Twins and higher multiple births. London: Rowland Phototype setting limited, 1992:55-67.
6. Windham GC, Bjerkedal T. Malformations in twins and their siblings. Acta Genet Med Gemellol 1984;38:87-95.
7. Schinzel AAGL, Smith DW, Miller JR. Monozygotic twinning and structural defects. J Pediatr 1979;95:921-30.
8. Filler RM. Conjoined twins and their separation. Semin Perinatol 1986;10:82-91.
9. Sanders RC, Blackmon LR, Hogge WA, Wulfsberg EA. Structural fetal abnor-malities. Baltimore: Mosby, 1996:221-7.
10. Chitrit Y, Zorn B, Filidori M, Robert E, Chasseray JE. Cloacal extrophy in MZ twins detected through antenatal ultrasound scanning. J Clin Ultrasound 1993;21: 339-40.
11. Windham GC, Sever LE. Neural tube defects among twin births. Am J Hum Genet 1982;34:988-98.

12. Windham GC, Bjerkedal T, Sever LE. The association of twinning and neural tube defects. Acta Genet Med Gemellol 1982;31:165-72.
13. French CA, Bieber FR, Bing DH, Genest DR. Twins, placentas, and genetics: acardiac twinning in a dichorionic, diamniotic, monozygotic twin gestation. Hum Pathol 1998;29:1028-31.
14. Van Allen M, Smith D, Shepard T. Twin reversed arterial perfusion (TRAP) sequence: A study of 14 twin pregnancies with acardius. Semin Perinatol 1983;7:285-9.
15. Phelan MC, Geer JS, Blackburn WR. Vascular anastomosis leading to amelia and cutis aplasia in dizygotic twin pregnancy. Clin Genet 1998;53:126-30.
16. Entezami M, Runkel S,Sarioglu N, Hese S, Weitzel HK. Diagnostic dilemma with elevated level of alpha-fetoprotein in an undiagnosed twin pregnancy with a small discordant holoacardius acephalus. Am J Obstet Gynecol 1997;177:466-8.
17. Hansen LM, Donnenfeld AE. Concordant anencephaly in monoamniotic twins and an analysis of maternal serum markers. Prenat Diagn 1997;17:471-3.
18. Coleman BG, Grumbach K, Arger PH, Mintz MC, Arenson RL, Minnuti M, Gabbe SG. Twin gestation: Monitoring of complications and anomalies with ultrasound. Radiology 1987;165:449-53.
19. Neilson JP, Hood VD, Cupples W, Gibson AA, Ferguson-Smith MA. Detection by ultrasound of abnormality in twin pregnancies during the second trimester. Br J Obstet Gynaecol 1982;89:1035-40.
20. Hanson JW. Incidence of conjoined twinning. Lancet 1975;2:1957-9.
21. Barth RA, Filly RA, Goldberg JD. Conjoined twins: prenatal diagnosis and assessment of associated malformations. Radiology 1990;177:201-7.
22. Deter RL, Sefos T, Harrist RB, Hill RM. Detection of intrauterine growth retardation in twins using individualized growth assessment. Evaluation of growth outcome at birth. J Clin Ultrasound 1992; 20:573-5.
23. Frints SG, de Die-Smulders CE, Hasaart TH. Anencephaly in monozygotic twins and recurrence risk. Prenat Diagn 1998;18:867-9.
24. Al-Malt A, Ashmead G, Judge N. Color-flow and Doppler velocimetry in prenatal diagnosis of acardiac triplet. J Ultrasound Med 1991;10:341-5.
25. Benson CB, Bieger FR, Genest DR. Doppler demonstration of reversed umbilical blood flow in an acardiac twin. J Clin Ultrasound 1989;17:291-5.
26. Timor-tritsch IE, Rottem S. Transvaginal sonography. 2nded. New York: Elsevier, 1991:361.
27. Berg KA, Clark EB, Astemborski JA. Prenatal detection of cardiovascular malformation by echocardiography: an indication for cytogenetic evaluation. Am J Obstet Gynecol 1988;159:477-81.
28. Copel JA, Cullen MT, Grannum PA, Hobbins JC. Invasive fetal assessment in the antepartum period. Obstet Gynecol Clin North Am 1990;17:201-3.
29. Chervenak FA, Isaacson G, Blakemore KJ, et al. Fetal cystic hygroma: cause and natural history. N Engl J Med 1983; 309:822-5.
30. O'Neill JA, Holcomb GW, Schnaufer L. Surgical experience with thirteen conjoined twins. Ann Surg 1988;208:299-312.
31. McCurdy CM Jr, Childers JM, Seeds JW. Ligation of the umbilical cord of an acardiac-acephalus twin with an endoscopic intrauterine technique. Obstet Gynecol 1993;82:708-11.
32. Fries MH, Goldberg JD, Golbus MS. Treatment of acardiac-acephalus twin gestations by hysterotomy and selective delivery. Obstet Gynecol 1992;79:601-4.
33. Holzgreve W, Tercanli S, Krings W, Schuierer G. A simpler technique for umbilical cord blockade of an acardiac twin. N Engl J Med 1994;331:56-7.
34. Sebire NJ, Sepulveda W, Hughes KS, Noble P, Nicolaides KH. Management of twin pregnancies discordant for anen-cephaly. Br J Obstet Gynecol 1997;104:216-9.
35. Lipitz S, Meizner I, Yagel S, Shapiro I, Achiron R, Schiff E. Expectant management of twin pregnancies discordant for anencephaly. Obstet Gynecol 1995;86:969-72.
36. Moore TR, Gale S, Benirschke K. Perinatal outcome of forty-nine pregnancies complicated by acardiac twinning. Am J Obstet Gynecol 1990;163: 907-12.
37. Kurauche O, Ishida T, Ohno Y, Ando H, Nomura S, Mizutani S, Tomoda Y. Serial fetal heart rate monitoring in monozygotic twin, one of which was anencephalic. Arch Gynecol Obstet 1995;256:53-6.
38. Kurauchi O, Ohno Y, Mizutani S, Tomoda Y. Longitudinal monitoring of fetal behavior in twins when one is anen-cephalic. Obstet Gynecol 1995;86:672-4.
39. Franceschini P, Licata D, Guala A, Di Cara G, Signorile F. Long first metacarpal in monozygotic twins with probable Baller-Gerold syndrome. Am J Med Genet 1998;80:303-8.
40. Courtens W, Grossman D, Van Roy N, Messiaen L, Vamos E. Noonan-like phenotype in monozygotic twins with a duplication-deficiency of the long arm of chromosome 18 resulting from a maternal paracentric inversion. Hum Genet 1998;103:497-505.