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태아 심장종양의 산전 진단과 산후 결과

연세대학교 의과대학 산부인과학교실

남가현 · 황한성 · 곽동욱 · 박용원 · 김영한

Fetal cardiac tumor: Prenatal diagnosis and postnatal outcome

Ka Hyun Nam, M.D., Han-Sung Hwang, M.D., Dong-Wook Kwak, M.D., Yong-Won Park, M.D., Young-Han Kim, M.D.

Departments of Obstetrics and Gynecology, Yonsei University College of Medicine, Seoul, Korea

Objective: The objective of this study was to evaluate the ultrasonographic appearance of suspected fetal cardiac tumor and their evolution until delivery and in the postnatal period, and to document the associated problems including tuberous sclerosis.

Methods: We retrospectively reviewed the medical records of all cases born in Yonsei University Health System, Seoul, Korea, between September 1996 and August 2006, and diagnosed as fetal cardiac tumor prenatally.

Results: 10 cases were found in all medical records. The mean age of the mothers on delivery was 30.2±2.4 and the mean gestational age on diagnosis was 30.6±5.4 weeks. The cardiac tumors were single in five cases and multiple in the other five cases. The size ranged from 7 to 34mm. Most of the tumors were located in right ventricle (RV, n=9), left ventricle (LV, n=6), but they also located in interventricular septum (IVS, n=4), right atrium (RA, n=1). In one case, fetal arrhythmia was found, which was normalized in two days after birth, and in another case, mild intracardiac flow obstruction was noted. The duration of postnatal follow-up ranged from 2 months to 36 months (mean, 18.9±13.1 months). In most cases the tumor masses decreased after birth (n=6), but had no change in utero (n=5). Three of them were diagnosed as tuberous sclerosis after birth, and none of them needed surgical intervention.

Conclusion: Fetal cardiac tumors and their effect on the fetal cardiac function could be well evaluated by two-dimensional and Doppler echocardiography. The fetal cardiac tumors may have little effect on the fetal well being both prenatally and postnatally from the cardiovascular standpoint in most affected fetuses, but are important in the early diagnosis of tuberous sclerosis and in suggesting careful follow-up and management.

Key Words: Cardiac tumor, Tuberous sclerosis

Introduction

Primary cardiac tumors are rare, with an estimated incidence of 0.27% among pediatric autopsies.[1] The Rhabdomyomas, fibromas, myxomas and teratomas constitute the most common cardiac tumors in the 1 to 15 years-old group and have a malignant attitude in less than 10% of the cases.[2] The most common type of cardiac tumor identified in infancy and childhood is rhabdomyoma. In gross appearance, rhabdomyomas usually present as circumscribed non-encapsulated lesions appearing as white areas with lobulated nod-

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교신저자 : 김영한
E-mail : yhkim522@yumc.yonsei.ac.kr

ules. Their more common sites are the ventricles but they may occur in every area of the heart. Their size may vary from a few millimeters to several centimeters (up to 9 cm). Rhabdomyomas are often multiple, sometimes consisting of numerous miliary nodules measuring less than 1 mm; in these instances the term "rhabdomyomatosis" has been used.[3]

Because many affected infants have no cardiac symptoms, cardiac rhabdomyomas not associated with tuberous sclerosis may go unrecognized. Therefore, the true incidence of cardiac rhabdomyoma in infants and children and the frequency of the associated tuberous sclerosis in all affected infants remain unclear.[4]

As is true after birth, cardiac rhabdomyomas are by far the most common cardiac tumor diagnosed in utero.[2] However, the prenatal diagnosis of cardiac rhabdomyoma most often occurs after referral for the finding of a cardiac tumor or fetal dysrhythmia on routine obstetrical ultrasound assessment without other obvious features of tuberous sclerosis at the time of diagnosis. Knowledge of the outcome of affected fetuses and the true incidence of tuberous sclerosis in fetal cardiac rhabdomyoma is critical for correct obstetrical management and for complete parental counseling.

Therefore, the objective of this study was to evaluate the ultrasonographic appearance of suspected fetal cardiac tumor and their evolution until delivery and in the postnatal period, and to document the associated problems including tuberous sclerosis.

Materials and Methods

We retrospectively reviewed the medical records of all cases born in Yonsei University Health System, Seoul, Korea, between 1996 and 2006, and diagnosed as fetal cardiac tumor prenatally.

We documented the mother's age at referral, the gestational age at diagnosis, the gestational age at birth, the types of delivery, the gender of the fetus, birth weight, Apgar score, and maternal history. Particular attention was paid to the thorough ultrasonographic findings and the fetal echocardiographic assessment including prenatal and postnatal tumor location, number, size, and hemodynamic effect, the presence of fetal arrhythmia, and postnatal clinical course. The postnatal clinical courses included cardiac symptoms, tumor size changes, associated tuberous sclerosis, and associated other cardiac anomalies. Clinical outcomes included seizure, and developmental delay. None of the cases were available with histologic diagnosis.

The diagnosis of tuberous sclerosis was based on the criteria established at the 1998 Tuberous Sclerosis Complex Consensus Conference.[5] Because most of the criteria cannot be diagnosed prenatally, the diagnosis of tuberous sclerosis was made postnatally.

Results

10 cases were found in all medical records, and all of them were supposed to be rhabdomyomas. Only in one case (No. 5), the tumor was found after birth, on the day of referral. In another case (No. 2), the patient refused all the postnatal evaluation. The mean age of the mothers on delivery was 30.2±2.4 weeks and the mean gestational age on diagnosis was 30.6±5.4 weeks.

There were no remarkable differences regarding gestational age at birth, types of delivery, gender, birth weight, APGAR scores of fetus, and maternal history. Of the 10 cases, six infants were born with spontaneous vaginal delivery, and four required cesarean section (all of them for maternal indications such as cephalopelvic disproportion, prior cesarean section, multifetal pregnancy, placental abruption, but not for

Table 1. Pregnancy outcomes of 10 cases of fetal cardiac tumors

No	Maternal Age (years)	Gestational age at Dx (weeks)	Gestational age at birth (weeks)	Type of delivery	Gender	Weight (grams)	APGAR (1/5 min)	Maternal History
1	31	36+2	40+3	VD	Female	3,380	8/9	Not commentable
2	30	31+0	36+1	c/sec	Male	2,410	8/9	twin, preeclampsia, placental abruption
3	31	24+6	37+4	VD	Male	3,000	7/8	Hyperthyroidism
4	32	39+1	39+4	VD	Male	3,620	7/8	Not commentable
5	35	25+5	25+5	c/sec	Female	790	1/2	Twin, endometriosis
6	31	23+5	40+3	c/sec	Male	3,460	6/8	CPD
7	27	26+0	39+1	VD	Female	3,030	7/8	Not commentable
8	28	33+3	38+1	VD	Female	2,990	8/9	Not commentable
9	30	29+0	38+5	c/sec	Male	4,000	8/8	prior c/sec
10	27	37+4	40+2	VD	Male	2,990	7/9	Not commentable

VD: vaginal delivery, c/sec: cesarean section, CPD: cephalopelvic disproportion, Dx: Diagnosis.

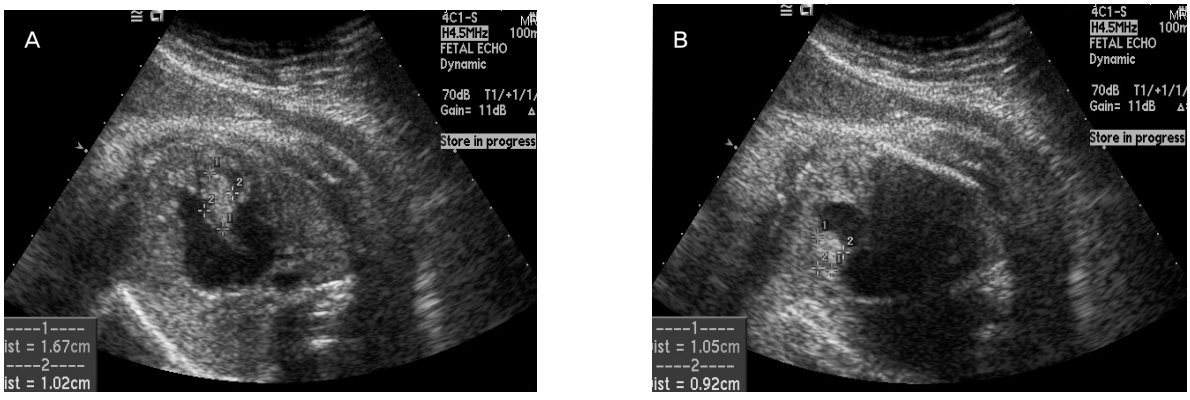

Fig. 1. The prenatal sonographic findings of fetal rhabdomyomas of case No.10 (A) largest mass on the interventricular septum, (B) another mass on the posterior wall of LV.

fetal cardiac tumor). Six were male and four were female. None of the parents has family history of seizure or tuberous sclerosis. One mother (No. 2) has placental abruption, another (No. 3) has hyperthyroidism. Two of them (No. 2, 5) are one of the babies of twins. In nine cases the tumors were found on routine obstetric follow-up (Table 1).

In utero, the cardiac tumors were single in five cases and multiple in the other five cases (Fig. 1). One case diagnosed with single tumor prenatally turned out to have multiple tumors on postnatal echocardiogram and another case diagnosed with multiple tumors had single tumor postnatally. The size ranged from 7 to 34 mm. Most of the tumors were located in right ventricle (RV, n=9), left ventricle (LV, n=6), but they also located in interventricular septum (IVS, n=4), right atrium (RA, n=1). In one case, fetal arrhythmia was found, which was normalized in two days after birth, and in another case, mild intracardiac flow obstruction was noted (Table 2).

The duration of postnatal follow-up ranged from 2 months to 36 months (mean, 18.9±13.1 months). In most cases the tumor masses decreased after birth (n=6) (Fig. 2), but had no change in utero (n=5). Three

Table 2. Intrauterine involution of fetal cardiac tumors

No	No. and sites of tumors (before birth)	No. and sites of tumors (after birth)	Tumor size (mm)	Cardiac function disturbance	Intracardiac flows disturbance	Evolution in utero
1	3 (RV, RA)	1 (RV)	16→12	Yes →No	Yes →No	regression
2	3 (LV, RV)	-	27→-	No	No	-
3	2 (RV, IVS)	>3 (LV, RV, IVS)	17→21→26→32	No	Yes (mild)	aggravation
4	1 (LV)	>3 (LV, RV, IVS)	17→18	No	No	no change
5	-	1 (RV)	-→10→21	No	No	-
6	1 (RV)	1 (RV)	9→29	No	No	aggravation
7	1 (LV)	1 (LV)	11*9→ 10*3	No	No	no change
8	1 (RV)	1 (RV)	9*8→9*6	No	No	no change
9	2 (LV, IVS)	3 (LV, RV, IVS)	34→30	No	No	no change
10	6 (LV, RV, IVS)	10 (LV, RV, IVS)	17→18	No	No	no change

RA, Right atrium; RV, Right ventricle; LA, Left atrium; LV, Left ventricle; IVS, Interventricular septum.

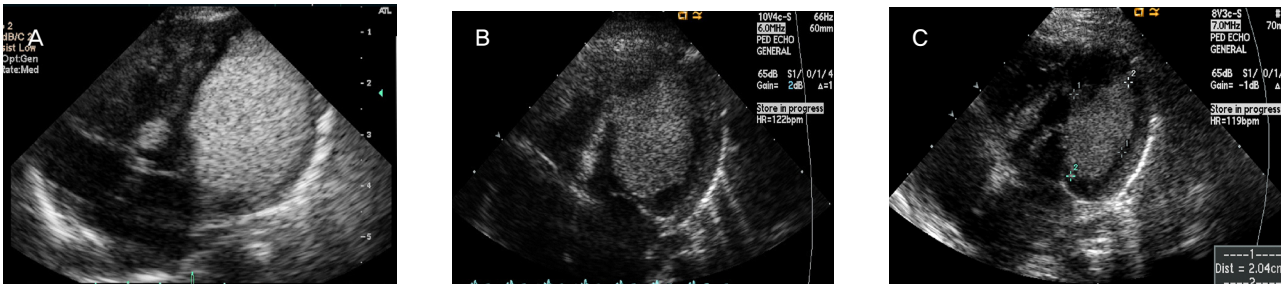

Fig. 2. The postnatal echographic findings of fetal rhabdomyomas of case No.9 (A) at birth, (B) 7 months, (C) at 13 months. The tumor sizes are slightly decreasing.

of them were diagnosed as tuberous sclerosis after birth, and none of them needed surgical intervention (Table 3). None of the babies enrolled in this study had postnatal comorbidity other than cardiac tumor, tuberous sclerosis, and cardiac anomaly, except one baby who was born at 25+2 gestational week. The baby suffered from infectious osteomyelitis, infectious enterocolitis, upper gastro-intestinal bleeding, acute renal failure, retinopathy of prematurity, hyaline membrane disease, and sepsis mostly supposed to come from prematurity.

Discussion

Rhabdomyoma is the most common type of cardiac tumor identified in utero, in infancy and during childhood.[2] Recent studies have indicated that cardiac rhabdomyomas do not cause hemodynamic compromise in most affected fetuses.[6] Rhabdomyomas are characterized by slow growth, with spontaneous postnatal regression, which has prompted an expectant approach to management.[6-8]

Fetal cardiac rhabdomyomas are easily diagnosed by ultrasound, due to their hyperechogenic appearance. The tumors appear as isolated or multiple hyperechoic nodular masses located in the cardiac cavities. Echocardiography allows accurate determination of the extent and location of the mass. Doppler study can also be useful to evaluate possible modification in the intracardiac hemodynamic.[3]

Table 3. Postnatal outcome of fetal cardiac tumors

No	Follow up (months)	Tumor regression after birth	Associated tuberous sclerosis	Associated other cardiac anomalies	Outcome
1	12	Yes	No	No	follow-up loss
2	0	-†	Yes	No	follow-up loss
3	36	Yes	No	Yes	normal development at 36 months
4	34	No	Yes	Yes	Seizure
5	32	No*	No	Yes	cerebral palsy, ASD
6	2	Yes	No	Yes	normal development at 2 months
7	14	Yes	No	Yes	normal development at 14 months
8	11	Yes	No	Yes	normal development at 11 months
9	13	Yes	No	Yes	normal development at 13 months
10	9	No	Yes	No	Seizure

*Aggravated, †No data is available.

The prenatal diagnosis of cardiac rhabdomyoma was first reported by De Vore et al in 1982.[9] Several other reports followed describing isolated cases.[7,10] In domestic studies, Hong et al. reported a case of fetal cardiac rhabdomyoma complicated with tuberous sclerosis in 2002,[11] and in 2006, Kim et al. documented the prenatal diagnosis and clinical outcome of affected fetuses with cardiac tumors in a single institution for the first time.[12] Our series also investigated the same features of fetal cardiac tumors and documented the incidence of tuberous sclerosis associated with them in a single institute for ten years. The overall results were not so different, but our study would be meaningful as a series case study. We were much more interested in hemodynamic compensation with accompanying cardiac anomalies.

In our study, fetal cardiac rhabdomyoma is identified in the third trimester in four cases and in the second trimester in the rests, which was different from other studies such as Bader's.[6] It might be due to the fact that the first diagnoses were not made in our institute. In all cases the patients were referred to our institute in suspicion of fetal cardiac tumor.

The number, size, and location of tumors showed no relation with tuberous sclerosis or with cardiac hemodynamics in our study. In some studies such as Lacey's, they emphasized on the position of tumor rather than the tumor size.[13] But in ours, the number of patient enrolled in the study was too small to find any statistical significance.

Fetal cardiac tumors and their effect on fetal cardiac function could be well evaluated by two-dimensional and Doppler echocardiography. Dysrhythmias may be observed in 16% to as high as 47% of cases and may necessitate prenatal or postnatal medical therapy,[2] but in our study, none of the case needed medico-surgical intervention.

The overall prenatal sonographic findings of fetal cardiac tumors were not markedly different from postnatal echocardiographic findings. In this study, in seven cases cardiac tumors were accompanied by other cardiac anomalies such as patent ductus arteriosus (PDA), atrial septal defect (ASD), and ventricular septal defect (VSD) which were resolved spontaneously after birth except in one case. These cardiac anomalies might be associated with hemodynamic compensation. Lesions obstructing inflow and/or outflow of one side of the heart in utero usually do not compromise fetal

cardiac output or cause congestive heart failure because of regional redistribution of fetal intracardiac blood flow through foramen ovale and ductus arteriosus.[14] The natural history of most tumors detected prenatally is favorable, with most tumors regressing beyond the third trimester[2,8,15]; however, in rare cases, there may be progression in utero.[16]

Tuberous sclerosis complex is an autosomal dominant multisystemic disorder with variable expressivity.[17] The population frequency is 1:10,000 to 1:6,000,[10] and about 80% are caused by de novo mutation.[5,17] The association between cardiac tumor and tuberous sclerosis is well known.[7,18,20] Previous reviews of the literature of antenatally diagnosed cardiac tumor,[7,19-21] which indicated an association of 50% to 58% with tuberous sclerosis. When we compared our fetal experience with prior studies, we have three tuberous sclerosis cases out of ten cases, but the statistical significance cannot be discussed due to the small study numbers. It has been suggested that fetuses with a single cardiac tumor are at lower risk for the development of tuberous sclerosis,[22] in our series of cardiac tumor, there were three cases with tuberous sclerosis and all of them were with multiple tumors. One of them was diagnosed with single tumor on prenatal fetal sonography but turned out to have multiple tumors on postnatal echocardiography. Given the lack of histologic evidence of rhabdomyoma, the diagnosis of cardiac tumor could not be confirmed.

In conclusion, fetal cardiac tumors and their effect on fetal cardiac function could be well evaluated by two-dimensional and Doppler echocardiography. The fetal cardiac tumor may have little effect on the fetal well being both prenatally, so single fetal cardiac rhabdomyoma may not be the indication of pregnancy termination, unless the affected fetuses had hemodynamic abnormalities or fetal hydrops. In our experience no correlation was found between the development of tuberous sclerosis and any particular sonographic sign, such as location, size and early development of the tumors, but due to the frequent association with tuberous sclerosis, these tumors can serve as a marker for this disease, particularly with multiple cardiac tumors or in families previously identified as genetic carriers. So, we emphasize the need for prenatal serial follow-up ehocardiographic evaluation and proper prenatal counseling for fetal cardiac tumor diagnosed prenatally.

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= 국문초록 =

목적: 본 연구의 목적은 분만 전 및 후의 태아 심장종양의 초음파상 모습을 평가하고 결절상 경화증 등 연관 문제들을 기술하고자 함이다.

방법: 1996년부터 2006년까지 단일 기관에서 산전에 태아 심장종양을 진단받고 출생한 환아들의 의무 기록을 후향적으로 분석하였다.

결과: 총 10예의 태아 심장종양 사례가 발견되었다. 출산 당시의 산모의 평균 연령은 30.2±2.4세였고, 진단 당시의 임신주수는 30.6±5.4주였다. 심장종양은 5예에서 단일 종괴였고 나머지 5예에서는 다수였다. 종괴의 크기는 7 mm에서 34 mm로 다양했다. 대부분의 종괴는 우심실에 위치하였으며 (n=9), 좌심실 (n=6), 심실 중벽 (n=4), 우심방 (n=1)에도 위치하였다. 1예에서 태아 부정맥이 있었으나 출생 후 2일째 정상화 되었고, 다른 1예에선 경도의 심혈류장애가 발견되었다. 생후 추적관찰기간은 2개월에서 36개월로 다양하였다 (평균 18.9±13.1개월). 대부분의 사례에서 종양의 크기는 생후 줄어들었다 (n=6). 하지만 태내에선 변화없는 경우가 많았다 (n=5). 10예 중 3예에서 결절성 경화증이 진단되었고 수술적 치료를 요한 경우는 없었다.

결론: 태아 심장종양과 태아 심장종양의 심장 기능에 대한 영향은 이차원 Doppler 심초음파로 충분히 평가할 수 있었다. 태아 심장종양은 출산 전과 후 모두에서 혈역학적 면에서는 태아 안녕에 거의 영향을 미치지 않았다. 하지만 태아 심장종양은 결절성 경화증의 조기 진단의 단서가 될 수 있으므로 관련 산모 및 태아에 대한 철저한 산전 상담 및 관리가 필요하다 하겠다.

중심단어: 태아 심장종양, 결절성 경화증