

# Fetal intrapericardial teratomas

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Fetal intrapericardial teratomas are rare and benign. However, they can be life-threatening owing to the complicated massive pericardial effusions, tamponade, or cardiorespiratory distress. The purpose of this review is to give an overview on clinical features, management and prognoses of fetal intrapericardial teratomas. The materials of this study were based on a comprehensive literature retrieval of fetal intrapericardial teratomas published in the past two decades. It was noteworthy that fetal pericardial/pleural effusions or ascites were detected since 19-week gestation, and tumors could be found since 21-week gestation. A growing trend of tumors was observed in more than half of the cases. Prenatal centesis and postnatal tumor resection were required in most of the cases. Fetoneonatal deaths (including fetal demise, termination of pregnancy and neonatal death) occurred in one-third of the cases. The neonatal survival rate was 59.4%. Symptomatic fetuses usually required perinatal maneuvers, such as pericardiocentesis, or thoraco-/pericardio-amniotic shunt in order to improve fetal hemodynamic status and prolong the pregnancy for lung maturity. Open fetal surgery and ex utero intrapartum treatment (EXIT) procedure can be considered, however, impact of EXIT procedure on later delivery remains uncertain. Postnatal operation is a curative and symptom-relieving method for those cases with prenatally diagnosed intrapericardial teratomas. As a result, the fetoneonatal outcomes are somewhat promising.

**Key words:** Pericardial teratoma, fetal surgery, fetus, hydrops.

Intrapericardial teratomas are rare primary cardiac tumors, accounting for 10% of mediastinal tumors of pediatric patients.<sup>1</sup> Pathologically, intrapericardial teratomas contain endodermic, mesodermic and neuroectodermic germinal layers.<sup>2</sup> Fetal intrapericardial teratomas are usually benign and asymptomatic, but sometimes complicated by cardiac compression, hydrops fetalis.<sup>3,4</sup> The teratomas can sometimes be fatal due to the associated massive pericardial effusions, cardiac compression,<sup>2</sup> and cardiorespiratory distress.<sup>5</sup> In such patients, pericardial effusions can be massive, and absence of pericardial effusions may mean that the pericardium is not affected by the tumor.<sup>6</sup> The clinical features, management and prognoses of fetal intrapericardial teratomas have not been sufficiently elucidated so far. The purpose of this article is to give an overview

of the clinical features, management and prognoses of fetal intrapericardial teratomas.

## Material and Methods

PubMed database and Yahoo! search engine were retrieved for publications reporting on fetal intrapericardial teratomas published in the past 20 years. The search terms included “(intra)pericardial teratoma” and “fetal/fetus/fetuses”. Bibliographic references were also tracked for the completeness of the literature retrieval.

Data were carefully extracted for details of the demographics of mother and fetus, and clinical features, management and prognoses of fetal intrapericardial teratomas.

Quantitative data were presented as mean  $\pm$  standard deviation with range and median

values. The intergroup differences were compared by independent samples *t*-test, and comparisons of frequencies were made by Fisher's exact test.  $p < 0.05$  was considered statistically significant.

The research was reviewed and approved by an institutional review board on January 10, 2018 (approval number 20180106), and that no informed consent of participation involved was applicable for this review article.

## Results

A total of 26 articles including 33 fetuses were collected,<sup>7-32</sup> and one of the fetuses was a twin.<sup>15</sup> Mothers aged  $29.0 \pm 6.0$  (range, 17-39; median, 29.5) years ( $n=24$ ), with a gravida of  $1.9 \pm 0.8$  (range, 1-3; median, 2) ( $n=19$ ), and a para of  $0.7 \pm 0.8$  (range, 0-2; median, 1) ( $n=17$ ). The gestational age at mother's presentation was  $26.1 \pm 5.0$  (range, 18.9-38; median, 26) weeks ( $n=30$ ).

The timing of presence or detection of fetal pericardial/pleural effusions or ascites was  $26.6 \pm 4.4$  (range, 19-36; median, 27) weeks ( $n=27$ ), the timing of increase of the effusions was  $28.3 \pm 5.1$  (range, 23-34; median, 28) weeks ( $n=5$ ). Hydrops fetalis was present in 18 (54.5%) cases. The timing of presence or detection of hydrops fetalis was  $27.4 \pm 4.4$  (range, 19-34; median, 29) weeks ( $n=18$ ). No difference was found between timing of pericardial/pleural effusions or ascites and timing of hydrops fetalis ( $p=0.6002$ ).

The diagnostic tools for the fetal intrapericardial teratomas were described in 26 (78.8%) cases: by ultrasound in 19 (73.1%), by fetal echocardiography in 13 (50%), by magnetic resonance imaging in 6 (23.1%) and by computed tomography in 2 (7.7%) cases.

The tumors were initially detected at  $34.1 \pm 14.0$  (range, 21-35; median, 30.8) weeks of gestation ( $n=23$ ). Tumor growth was observed in 19 (57.6%) cases. The initial size of the fetal tumors was  $26.2 \pm 4.6$  (range, 18.9-36; median, 26) mm ( $n=32$ ), and the neonatal tumor size was  $49.6 \pm 22.7$  (range, 24.1-130; median, 45) mm ( $n=19$ ). A significant tumor growth was seen from the fetal to the neonatal period ( $p < 0.0001$ ).

The arising sites of the tumors were described in 21 (63.6%) cases: they were arising from

the ascending aorta in 10 (47.6%) cases, from the surface of the right atrium in 5 (23.8%) cases, from the aorta and pulmonary artery/great vessels in 3 (14.3%) cases, from the pericardium in 1 (4.8%) case, from right atrium, the right ventricle and the ascending aorta in 1 (4.8%) case, and they surrounded the innominate vein, arch vessels and transverse aortic arch in 1 (4.8%) case.

Tumor compression was observed in 14 (42.4%) cases, and most of the structures compressed were right heart chambers (Table I). Only 1 (3.0%) fetus was associated a cardiac structural defect -- patent ductus defect. Reaccumulation of the effusions developed in 9 (27.3%) cases after the initial management for  $1.9 \pm 1.2$  (range, 1-4; median, 1) time(s) ( $n=9$ ).

The delivery time was  $32.2 \pm 5.0$  (range, 19-40; median, 32) weeks of gestation ( $n=25$ ). The delivery modes were described in 26 cases: cesarean section in 19 (73.1%) cases (one of the fetus was a twin), vaginal delivery in 3 (11.5%) cases and termination of pregnancy in 4 (15.4%) cases. Gender was described for 14 (56%) neonates: 9 (64.3%) were females and 5 (35.7%) were males ( $\chi^2=2.29$ ,  $p=0.131$ ). Their birth weight was  $2255.2 \pm 816.2$  (range, 1100-4330; median, 2160) g ( $n=19$ ).

Twenty-five (75.8%) fetuses received treatments for the teratomas. Prenatal centesis and postnatal tumor resection were required in most of the cases (Table II).

Pathology of the teratomas was reported for 28 (84.8%) cases: 11 (39.3%) were mature, 6

Table I. Tumor Compressions.

Adjacent structure compressed by tumor	<i>n</i> (%)
RA, RV, superior vena cava	4 (28.6)
RA, superior vena cava	2 (14.3)
Aorta, systemic venous return	1 (7.1)
Heart	1 (7.1)
RA	1 (7.1)
RA, RV	1 (7.1)
Right heart chambers	1 (7.1)
Superior vena cava	1 (7.1)
Trachea, esophagus	1 (7.1)
Lung	1 (7.1)

RA: right atrium; RV: right ventricle.

**Table II.** Management of Choices for Intrapericardial Teratomas of 25 Fetuses (55 Occasions).

Management	n (%)	Time (gestational week or days of life)	Amount by centesis or drainage (ml)
Antenatal	27 (49.1)		
Drug	4 (14.8)		
Steroids	4 (100)		
Maneuver	23 (85.2)		
Pericardiocentesis	14 (60.9) (18 times)	30.0 ± 3.5	40.6 ± 23.9
Pericardiocentesis & thoracocentesis	2 (8.7)	29, 30	8, 22
Pericardial and pleural fluid drainage	1 (4.3)	25.9	10, 15
Amniotic fluid drainage	1 (4.3) (3 times)	31.1, 32.1, 32.9	1350, 1500, 1600
Pericardioamniotic shunt	3 (13.0)	26.1 ± 2.8	30
Thoracoamniotic shunting	2 (8.7)	29, 30.7	
Fetal	3 (5.5)		
Fetal surgery	1 (33.3)	24	
EXIT	2 (66.7)	24.1, 31	
Postnatal	25 (45.5)		
Drug	3 (12)		
Nonsteroid	1 (33.3)		
Anti-inflammatory treatment	1 (33.3)		
Intratracheal surfactant	1 (33.3)		
Maneuver	2 (8)		
Pleural effusion drainage	1 (50)		
Cardiac effusion drainage	1 (50)		
Tumor resection	20 (80)	7.2 ± 10.6	

EXIT: ex utero intrapartum treatment

(21.4%) were immature, 3 (10.7%) were mixed mature and immature with predominance of mature cells and 8 (28.6%) were unspecified teratomas.

The neonates were at a follow-up of  $11.5 \pm 9.4$  (range, 1-36; median, 10) months (n=12). Fetoneonatal prognosis was described for 32 (97.0%) cases: there were 11 (34.4%) fetoneonatal deaths including 5 (45.5%) fetal demises, 2 (18.2%) neonatal deaths and 4 (36.4%) terminations of pregnancies. In the remaining 21 (65.6%) cases, 9 (42.9%) had a neonatal comorbidity, 12 (57.1%) were event-free survivals, and 2 (9.5%) died of neonatal comorbidity. The survival rate was 59.4% (19/32). The neonatal comorbidities were respiratory distress in 3 (33.3%), bronchopulmonary dysplasia in 2 (22.2%) (one of them was associated with poor hemodynamics), bronchostenosis in 1 (11.1%), pulmonary hypoplasia and extreme cardiomegaly

in 1 (11.1%), gastrointestinal perforation on day 11 requiring an ileostomy in 1 (11.1%), and acute cardiac failure with respiratory insufficiency in 1 (11.1%), respectively. The discharge date was described in 5 (23.8%) neonates, and it was  $56.2 \pm 77.7$  (range, 2-181; median, 7) days (n=5).

$\alpha$ -fetoprotein levels were reported in 5 fetuses with intrapericardial teratoma. The results generally showed a highest  $\alpha$ -fetoprotein level after birth and a gradually decreased  $\alpha$ -fetoprotein level with time (Table III).

## Discussion

Kulthe et al.<sup>5</sup> reported an infantile intrapericardial teratoma presenting with recurrent pericardial effusion and tamponade. Bader et al.<sup>8</sup> stated that hydrops occurred in 77% of affected fetuses, and no correlation was found between tumor size and progressive hydrops.

Table III.  $\alpha$ -Fetoprotein in Fetuses With Intrapericardial Teratoma ( $\mu\text{g/L}$ ).

Author	At birth	2 day	2 week	Discharge	Further	1 m	2 m	3 m	4 m	5 m	6 m
Agarwal et al. <sup>7</sup>		60500					2753		91		
Cetrano et al. <sup>10</sup>		70885		7053	1743						
Iacona et al. <sup>18</sup>	350000					2103000		169000			
Molina-Mora et al. <sup>22</sup>	96753										
Roy et al. <sup>26</sup>		91853	66000					265	225	171	139

m: month

In infantile patients, signs of respiratory distress, cyanosis, superior vena cava obstruction, or cardiac tamponade should arouse the suspicion of an intrapericardial teratoma.<sup>5</sup> Two-dimensional echocardiography is a golden standard diagnostic modality for intrapericardial teratomas, but magnetic resonance imaging may be helpful in outlining the relationships between the tumor and the adjacent structures.<sup>2</sup> Nowadays, prenatal ultrasound and fetal echocardiography have greatly facilitated the early diagnosis of fetal intrapericardial teratomas.<sup>33</sup> Doppler may help indicating the risks of hydrops fetalis.<sup>8</sup>

An elevated  $\alpha$ -fetoprotein level in maternal serum and amniotic fluid is a reliable indicator of a fetal abnormality, such as neural tube defects, omphalocele, gastroschisis and sacrococcygeal teratoma.<sup>34</sup> The  $\alpha$ -fetoprotein was reported to be close to 100,000  $\mu\text{g/L}$  at birth and decreases after an inverse logarithmic curve to approximately 100  $\mu\text{g/L}$  at 1 month of life, and then to a normal level at 1 year of age. It has been suggested that the rapidity of  $\alpha$ -fetoprotein decay after resection of intrapericardial teratoma is a more accurate prognostic factor in immature teratomas than any isolated value.<sup>26</sup>

As for the prognoses of fetal intrapericardial teratomas, 42% died perinatally with 6 fetal and 4 neonatal deaths, and 58% survived.<sup>8</sup> Nassr et al.<sup>33</sup> summarized the data of 67 fetuses with intrapericardial teratoma, and 6 non-hydrops and 20 hydrops fetuses warranted fetal interventions, including 15 pericardiocenteses alone (57.6%), pericardiocentesis followed by thoracocentesis and then placement of a thoraco-amniotic shunt (n=1), pericardio-amniotic shunt (n=3), thoracocentesis (n=1), laser ablation (n=2, additional pericardiocentesis performed in one of these cases), ex utero intrapartum treatment (EXIT) to resection (n=1), and open fetal surgery (n=3). The survival rate of non-hydrops fetuses was much better than that of hydrops fetuses (95.2% (20/21) vs. 58.3% (28/46)).

Perinatal maneuvers aim at improving fetal hemodynamic status and prolonging the pregnancy.<sup>33</sup> Bader et al.<sup>8</sup> summarized 11 of 31 fetal cases receiving fetal pericardial drainage at 22-33 week gestation: 4 (36.4%) cases required multiple pericardiocenteses

due to reaccumulation of fluid, 6 (54.5%) cases received only once pericardiocentesis.<sup>8</sup> Moreover, prenatal pericardio-amniotic shunt ensures continuous drainage of the pericardial effusions, avoids repeated pericardiocentesis and allows lung expansion.<sup>8</sup>

Open fetal surgery should be reassessed concerning the risk of a large hysterotomy during the operation.<sup>33</sup> EXIT to tumor resection was once reported to obtain a promising outcome, but the impact of the procedure on later delivery and elective operation remains uncertain.<sup>33</sup> Postnatal operation is almost curative and provides prompt relief of symptoms.<sup>5</sup> It was reported that about 90% of intrapericardial teratomas were attached to the aorta or main pulmonary artery.<sup>35</sup> Therefore, complete surgical excision can be performed with ease without the aid of cardiopulmonary bypass.<sup>35</sup> But in the present review, we noted two cases were operated on on-pump due to tumor-related aortic obstruction, profound hypotension and aortic wall defect repair<sup>12</sup> or due to bradycardia and hypotension.<sup>31</sup> No recurrence has been reported after complete tumor resection.<sup>35</sup>

Fetal intrapericardial teratomas are rare and benign. However, they can be life-threatening owing to the associated massive pericardial effusions, tamponade, or cardiorespiratory distress. Symptomatic fetuses usually required perinatal maneuvers, such as pericardiocentesis, or thoraco-/pericardio-amniotic shunt in order to improve fetal hemodynamics and prolong the pregnancy for lung maturity. Open fetal surgery and EXIT can be considered but the impact of EXIT procedure on later delivery remains uncertain. Postnatal operation is a curative and symptom-relieving method for those cases with prenatally diagnosed intrapericardial teratomas. It has been proved that fetoneonatal outcomes are promising.

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