Nontrophoblastic placental tumors

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Abstract

The aim of the study was to investigate potential influence of placental tumors on fetal outcome. The study comprised 10 cases of placental tumors. The analysis included the sonographic assessment of the tumor, signs of fetal anemia, as well as signs of hemodynamic disturbances or heart failure, and intrauterine treatment. The fetal hemodynamic was examined on the basis of Doppler blood flow in the umbilical artery and vein, middle cerebral artery, and ductus venous. The evaluation of fetal heart included the measurement of heart size, blood flow through cardiac valves and the assessment of fetal heart function based on cardiovascular score. The fetal outcome was also assessed according to birthweight, gestational age at delivery, pH, Ap score at 5th minute, abnormal neurological development and the need of intrauterine therapy. Ten cases of placental tumors were prenatally detected from 1999 to 2011. Among them 7 cases of hypoechogenic, non-vascularized cysts were identified and these neither effected the hemodynamics nor complicated fetal outcome. The vascularized tumors (chorioangioma) were the cause of severe anemia and hemodynamic disturbances and these led to fetal cardiac heart failure. In all cases of vascularized tumors from 2–3 intrauterine transfusion were performed. Rich vascularized tumors (chorioangioma) may cause hemodynamic disturbances and fetal heart failure. This may require intrauterine treatment and may result in abnormal fetal outcome and neurological development.

Abbreviations:

DV	- ductus venosus
HC/ThC	- heart circumference /thoracic circumference
Htc	- hematocrit
MCA	- the middle cerebral artery
MCA-PSV	- peak systolic velocity in the middle cerebral artery
PI	- pulsatility index
Pts	- points
UA	- the umbilical artery
UV	- the umbilical vein

CASE REPORT

INTRODUCTION

Chorioangiomas belong to the group of non-trophoblastic tumors. Non-trophoblastic tumors are always benign. In most cases they are small, less than 4 cm in diameter, asymptomatic and usually diagnosed accidentally during routine ultrasound or histopathologic examinations (Fox & Sebire 2007). Although larger tumors, especially angiomas measuring more than 4 cm, are rarely seen in obstetric practice, yet they are clinically significant because they are associated with a number of pregnancy complications. Large size neoplasms have a great impact on hemodynamics of the fetal cardiovascular system. This implies that severe complications, such as: polyhydramnios, anemia, heart failure and even intrauterine fetal death may develop (Gruca-Stryjak *et al.* 2011a,b; Hamid *et al.* 1993). Therefore, prenatal diagnosis (Guschmann *et al.* 2003; Hamid *et al.* 1993; Zanardini *et al.* 2010; Zienab & Heller 2010) should be performed as early as possible and novel intrauterine treatment (Quarello *et al.* 2005) should be implemented to minimize the risk for the developing fetus.

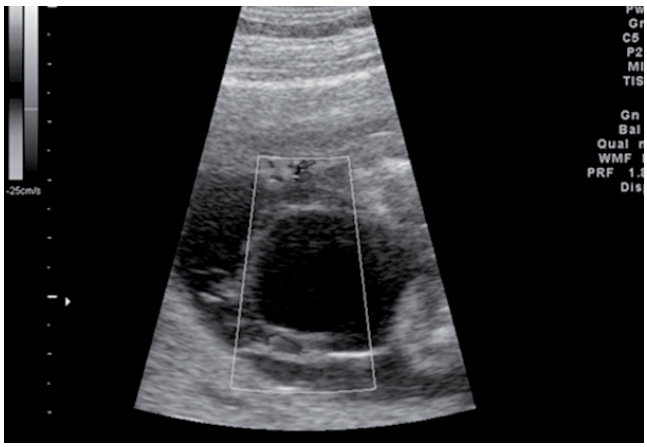

Fig. 1. Hypoechogenic, unicellular placental lesion with thin wall in the region of the umbilical cord insertion.

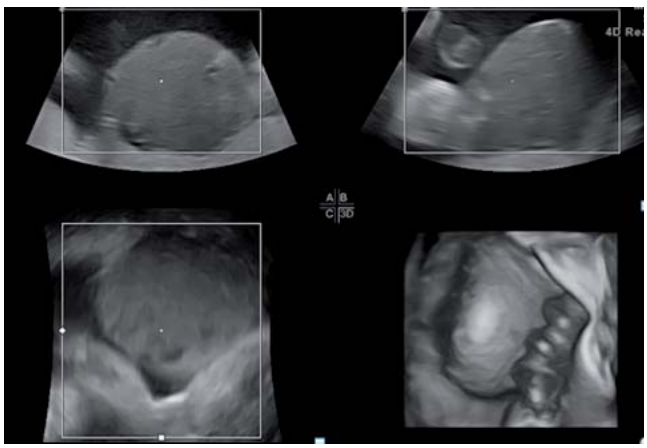

Fig. 2. A large, solid mass of the tumor bulges from the placental surface to the amniotic cavity close to the placental attachment of the umbilical cord at 31 week'gestation (case 5)

The aim of this study was to investigate a potential influence of placental tumors on fetal outcome.

MATERIAL AND METHODS

The study included 10 cases of placental tumors; among them we distinguished 3 tumors with rich vascularization and 7 cases of hypoechogenic cysts. All of them were located close to placental attachment of the umbilical cord. The analysis included the sonographic assessment of the tumor (size, echogenicity, vascularization), signs of fetal anemia, as well as signs of hemodynamic disturbances or heart failure. In case of fetal anemia and intrauterine treatment, the number of transfusions was also assessed. Fetal hemodynamics was examined on the basis of Doppler blood flow velocimetry in the umbilical artery (UA) and vein (UV), the middle cerebral artery (MCA), and ductus venosus (DV). The evaluation of fetal heart included the measurement of heart size, blood flow through cardiac valves (tricuspid, mitral, pulmonary and aortic valve) and the assessment of fetal heart function based on cardiovascular score (Huhta 2005). Fetal outcome was also assessed with relation to birthweight, gestational age at delivery, pH, Ap score at 5th minute, abnormal neurological development and the need of intrauterine therapy.

RESULTS

During the 10-year period, from 1999 to 2011, 10 cases of placental tumors were detected prenatally at Department of Perinatology and Gynecology. In 7 cases hypoechogenic, unicellular lesions with thin wall and capsule were identified. The lesions were similar to cysts (Figure 1). The size of the tumors ranged from 4 to 7 cm. Vascularization within the lesions was not observed or poor vascularization could be occasionally observed in the capsule. The blood flow in the vessels of the tumor's capsula was high-resistant. These types of tumors did not effect the hemodynamics in the fetus and the fetal outcome was uncomplicated (Table 1).

In cases 2, 5 and 10 the diagnosis of large tumors with reach vascularization was made (Figure 2). The size of these neoplasms ranged from 8 to 10 cm in diameter (Table 1). These neoplasms were located in the placenta near the umbilical cord insertion (Figures 3, 4). Polyhydramnios was diagnosed in all these patients. The tumors were the cause of severe anemia and hemodynamic disturbances, which led to fetal cardiac heart failure. Increased peak systolic velocity in the middle cerebral artery (MCA-PSV), pulsatile umbilical venous flow velocity and abnormal blood flow within the fetal heart were observed (Table 2). Cardiomegaly, holosystolic tricuspid value regurgitation, regurgitation of the pulmonary artery valve were identified by echocardiography. The cardiovascular score was lower than in the cystic tumor group. In all cases of vascularized tumors intrauterine transfusion was performed (from 2

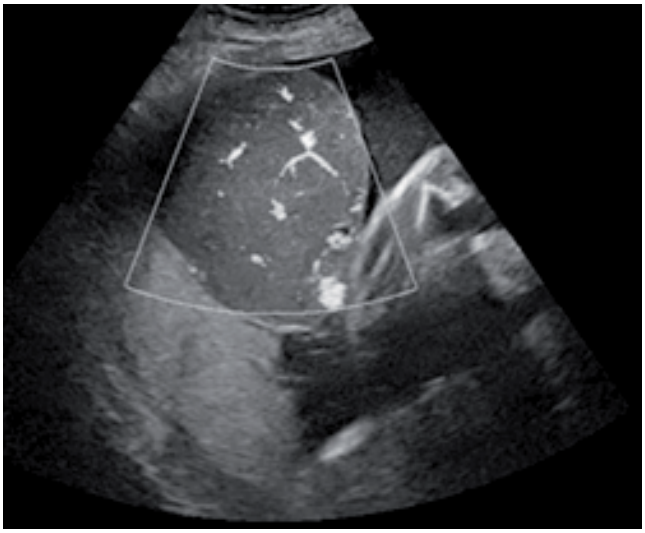

Fig. 3. Color Doppler imaging of the rich vascularization of the placental tumor (case 5).

Fig. 4. Hugh placental chorioangioma with conspicuous blood vessels after delivery at 36 week of gestation (case 5).

Tab. 1. Ultrasonographic signs of the tumor and fetal outcome.

Case	1	2	3	4	5	6	7	8	9	10
Gestational age at diagnosis (weeks)	18	30	22	28	31	17	26	30	20	24
Sonographic appearance 1. Hypoechogenic simple cyst 2. Hyperechogenic mass	1	2	1	1	2	1	1	1	1	2
Vascularization 1. no/within the capsule 2. rich, central vascularization	1	2	1	1	2	1	1	1	1	2
Size – mean diameter (cm)	4	10	5	4	8	7	3	9	3	7
Intrauterine therapy (number blood transfusions)	0	2	0	0	3	0	0	0	0	3
Fetal Htc		0.18			0.22					0.25
Apgar score in 5 minute (pts)	9	8	10	9	8	7	10	10	8	10
pH	7.19	7.35	7.42	7.38	7.17	7.25	7.22	7.32	7.46	7.31
Birth weight (g)	3210	2850	3570	3720	2670	3420	3700	4130	4210	2990
Gestational age at delivery (weeks)	37	37	40	39	36	39	40	40	38	36
Abnormal neurological development (yes/no)	no	no	no	no	yes	no	no	no	no	no

to 3). During intrauterine transfusion we were able to correct fetal anemia and all babies were born without hemodynamic problems. However, in case number 5 abnormal neurological development was observed. In cases 2, 5 and 10 the patomorphological examination confirmed chorionagioma. In this group patients delivered at 36–37 week's gestation, earlier than in the simple cyst group. The birthweight was also lower compared to the non-vascularized tumors group. In all remaining cases fetal outcome was uncomplicated.

The number of cases is to small to conclude. We may comment that the course of pregnancy with the large chorioangioma was complicated in all our cases and related to fetal anemia and hemodynamic disturbances.

DISCUSSION

This is a case series describing placental tumors with different influence on pregnancy course and fetal outcome. In this group three cases of chorioangioma was diagnosed. Chorioangiomas are the most common benign tumors of the placenta (Fox & Sebire 2007; Zanardini *et al.* 2010). Most of them are vascular tumors, usually single, small, encapsulated and intra-

Tab. 2. Fetal echocardiography and Doppler blood flow velocimetry in the selected vessels.

	1	2	3	4	5	6	7	8	9	10
Cardio/thoracic ratio (HC/ThC)	0.34	0.40	0.33	0.35	0.42	0.35	0.31	0.33	0.33	0.38
Mitral valve regurgitation	no	no	no	no	no	no	no	no	no	no
Tricuspid valve regurgitation	no	yes	no	no	yes	no	no	no	no	yes
Pulmonary valve regurgitation	no	yes	no	no	yes	no	no	no	no	no
Aortic valve regurgitation	no	no	no	no	no	no	no	no	no	no
Hyperdynamic circulation	no	yes	no	no	yes	no	no	no	no	yes
abnormal UA PI	no	no	no	no	no	no	no	no	no	no
MCA PSV MoM	< 1.5	1.8	< 1.5	< 1.5	1.6	< 1.5	< 1.5	< 1.5	< 1.5	1.6
UV pulsations	no	yes	no	no	yes	no	no	no	no	yes
abnormal DV PI	no	no	no	no	no	no	no	no	no	no
Cardiovascular score (pts)	10	6	10	9	6	9	10	10	10	6

placental. Small tumors in most cases are primarily clinically asymptomatic and, more importantly, their presence does not typically have any impact on fetal development. Large or giant placental chorioangiomas, defined as measuring more than 5 cm in diameter, are quite rare with incidence rate of 1:3500 do 1:9000 (Fox & Sebire 2007; Hamid *et al.* 1993; Quarello *et al.* 2005). Chorioangiomas measuring more than 2 cm are relatively easy to identify prenatally during routine ultrasound examination. Their sonographic appearance may be similar to placental hematomas, and in such case the use of color Doppler imagining can facilitate the diagnosis as the imaging makes the characteristic blood flow within the tumor apparent. Most chorioangiomas are localized underneath the chorionic plate near the insertion of the umbilical cord and they often protrude into the amniotic cavity (Gruca-Stryjak *et al.* 2011a,b). Chorioangioma may arise along the umbilical cord, in which case it derives from umbilical vessels. Its most common localization is near the placental end and it is usually surrounded by edematous Wharton's jelly. In cases of localization in the area of fetal-end umbilical cord, the neoplasm is totally detached from large vessels by connective tissue. Umbilical cord angioma usually has its own peduncle and capsule (Guschmann *et al.* 2003). In our study chorioangiomas ranged from 7 to 10 cm and were located close to the placental attachement of the umbilical cord (Figure 2). Placental chorioangioma is typically represented on ultrasound as a well-defined echogenic mass bulging from the placental surface and consisting of solid and cystic components. Indeed, these cystic components are equivalents of enlarged blood vessels creating a dense vascular network (as we presented in case 2,5,10). On the basis of the blood flow within the mass, color Doppler imagining is considered to be a good sonographic marker and therefore, it can be used to differentiate vascular tumor from hematoma (Zienab & Heller 2010).

Chorioangioma has been referred to as a hamartoma-like, or a hyperplastic capillary lesion, rather than a true neoplasm. In histological terms, it consists of small blood vessels that are embedded within the stroma of enlarged placental villi and they are covered with a trophoblast layer (Guschmann *et al.* 2003). The neoplasm arises from the chorionic mesenchyme. This type of angioma can give various histopathologic pictures: 1-vascular (mature) type consists of a vascular network and poor stroma, 2-cellular (immature) type is made up of immature mesenchymal cells, 3-degenerative type consists of myxoid changes, calcification, hemosiderin, and infarcts (Guschmann *et al.* 2003; Zienab & Heller 2010). If myxoid changes in the tumor are predominant, the tumor is called angiomyxoma.

From the practical point of view, only large chorioangiomas are significant. Their presence may lead to the development of complications. The number of feto-maternal complications may include fetal anemia and thrombocytopenia, polyhydramnios, cardiomegaly and fetal heart failure leading to non-immune hydrops, fetal growth restriction, preterm delivery, and maternal pre-eclampsia (Fox & Sebire 2007, Zanardini *et al.* 2010). In 1/3 of the cases with a large lesion, intrauterine fetal death may be expected. Hyperdynamic circulation caused by the fact that the fetus has to supply blood to the large neoplasm may cause a problem to a fetus such as hypoxia or malnutrition of the fetus. Arteriovenous fistula in the systemic circulation results in lower fetal cardiac afterload. This may in turn trigger hemodynamic compensation to maintain both fetal tissue perfusion and placental exchange. Insufficient reserve capacity of the fetal heart may deteriorate into congestive heart failure. Increased blood flow through the low resistance vascular channels could be an etiologic factor for the development of fetal heart failure (Hamid *et al.* 1993, Gruca-Stryjak *et al.* 2011a,b). So, in all cases of large chorioangioma the physician should focus on

the assessment of fetal hemodynamics to exclude or confirm symptoms of cardiomegaly and cardiac insufficiency. In all of our chorioangiomas hyperdynamic circulation was diagnosed and all fetuses required intrauterine therapy.

The possible reason of fetal anemia has been described as being related to fetomaternal hemorrhage, microangiopathic hemolysis or hemodilution (Hamid *et al.* 1993). Entrapment and destruction of fetal red blood cells and platelets flowing in the vascular network is a possible cause of hemolytic anemia. If at delivery the blood is not returned to the fetus before the umbilical cord has been clamped, the fetus may suffer from severe acute anemia. The large vascular tumor can act as a physiological and functional dead space. This may lead to uteroplacental insufficiency with subsequent chronic hypoxia, fetal distress, growth restriction or even intrauterine fetal death (Guschmann *et al.* 2003; Hamid *et al.* 1993).

Basing on the literature, every intrauterine fetal death was a consequence of the presence of a large chorioangioma and of the developing fetal heart failure (Zanardini *et al.* 2010; Hamid *et al.* 1993). The prematurity of the baby and the presence of diffuse angiomas in the placenta may also be responsible for intrauterine fetal demise (Querello *et al.* 2005).

In view of the well-known association between chorioangiomas and poor pregnancy outcome, appropriate treatment should be undertaken as soon as possible. If complications develop in the third trimester and the fetus is mature, planned delivery could be considered. However, most complications manifest themselves in the second trimester, at which time delivery is not an option. A number of treatment modalities have been discussed in the literature (Gruca-Stryjak *et al.* 2011a,b; Hamid *et al.* 1993; Lau *et al.* 2003; Nicolini *et al.* 1999; Querello 2005; Quintero *et al.* 1996). Intrauterine transfusion through cordocentesis is the most common treatment, yet, at best, it gives only temporary relief from anemia and does not correct the primary pathology (Gruca-Stryjak *et al.* 2011a,b). Since fetal red blood cells continue to be destroyed within the tumor, repeated transfusions are often necessary. Nevertheless, this procedure should be reserved for fetuses suffering from anemia or for hydropic fetuses. As polyhydramnios is the most frequent complication, a series of amniodrainage has been used with good results. Fetal heart failure can be treated by digoxin given to the mother (Querello *et al.* 2005). It must be stressed, however, that the procedures discussed do not treat the cause of the problem but only alleviate the symptoms.

There are some more aggressive approaches such as blocking vascular supply to the tumor presented in the literature. Quintero *et al.* suggested performing fetoscopic ligation and bipolar electrosurgery (Quintero *et al.* 1996). Another option may be the insertion of microcoils into the feeding arteries of chorioangioma in order to induce thrombosis and devascularization of the tumor (Lau *et al.* 2003). Moreover, injection of absolute alcohol into the tumor's veins induced severe endothelial damage and intravascular coagulation, thereby devascularizing the neoplasm (Nicolini *et al.* 1999).

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