Nontrophoblastic placental tumors

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Abstract

Primary placental and umbilical cord neoplasms can be divided into trophoblastic and nontrophoblastic tumors. Nontrophoblastic tumors are always benign, usually asymptomatic and they do not require performing any medical procedures during pregnancy. Chorangioma is the most common tumor in this group. The occurrence of giant chorangioma is associated with poor prognosis for the developing fetus and with complications in the mother. In this article we present an up-to-date information about nontrophoblastic placental tumors with particular focus on large placental chorangioma and on possible ensuing complications.

Key words: chorangioma, placental mass, ultrasonography, pregnancy outcomes, cardiac insufficiency

Introduction

Neoplastic lesions of the placenta can be divided into primary and secondary tumors. Secondary tumors, which are metastasis from other body organs, include: melanoma, lung cancer, breast cancer or lymphoma. From the histogenetical point of view, primary placental tumors can be divided into trophoblastic and nontrophoblastic neoplasms. The first group consists of neoplasms of trophoblastic disease’s origin: partial and complete hydatidiform mole, invasive mola, choriocarcinoma and placental site trophoblastic tumor. Chorangioma and teratoma belong to the group of nontrophoblastic tumors. Unlike the first group, nontrophoblastic tumors are always benign. In most cases they are small, less than 4 cm in diameter, asymptomatic and usually they are accidentally diagnosed during routine ultrasound or histopathologic examinations [1]. 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 neoplasmas 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 [5]. Therefore, a prenatal diagnosis [2-5] should be performed as early as possible and novel intrauterine treatment [6] should be implemented to minimize the risk for the developing fetus.

The aim of the present study is to present an up-to-date information about frequency, clinical significance, histopathologic origin and characteristics of nontrophoblastic placental tumors.

During the 10-year period from 2001 to 2011 in Department of Perinatology and Gynecology University School of Medical Sciences 7 cases of the placental tumor were prenataly detected. In 5 cases hypoechogenic, unicellular lesions with thin wall and capsula were identified. The lesions were similar to cysts. The size of the tumors ranged from 4 to 7 cm. Vascularization within the lesions was not observed. The blood flow in the vessels of the tumor’s capsula was high-resistent. This types of tumors did not effect on the hemodynamic system in the fetus. In 2 cases we diagnosed a large tumors with reach vascularization. The size of this neoplasms ranged from 8 to 10 cm in diameter. We observed reach, vascular network within the tumor. These neoplasms were located in the placenta near the umbilical cord insertion. Polyhydramnios was diagnosed in both pregnant patients. The tumors were the cause of severe anemia and hemodynamic disturbances, which led to fetal 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. Cardiomegaly, holosystolic tricuspid valve regurgitation, regurgitation of the trunk pulmonary valve were identified in echocardiography. In both cases intrauterine transfusion was performed. During intrauterine transfusion we were able to correct fetal anemia and both babies were born without hemodynamic problems.

Chorangioma

Chorangiomas are the most common benign tumors of the placenta [1-2]. They are vascular tumors, predominantly single, small, encapsulated and intraplacental. The neoplasmas are frequent in multiple pregnancy,
their estimated incidence being about 1%. In most cases they are primarily small and clinically asymptomatic and, more importantly, their presence does not typically have any impact on fetal development. Large or giant placental chorangiomas, arbitrarily defined as measuring more than 5 cm in diameter, are quite rare with incidence rate of 1 : 3500 to 1 : 9000 [1, 5-6]. They are frequently diagnosed prenatally by ultrasound imagining or in routine pathological examination (Fig. 1). Most chorangiomas are localized underneath the chorionic plate near the insertion of the umbilical cord and they often protrude into the amniotic cavity.

Chorangioma 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 oedematous 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 capsula [3, 7] (Fig. 3 and 4).

Chorangioma 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 [3]. 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 a poor stroma, 2-cellular (immature) type is made up of immature mesenchymal cells, 3-degenerative type consists of myxoidal changes, calcification, hemosiderin, and infarcts [3, 4, 7]. If myxoidal changes in the tumor are predominant, the tumor is called angiomyxoma. Sometimes muscle fibers or fibroblasts with collagen can be found within the stroma and then they are accordingly called angiomyoma and angiofibroma. Occasionally, we may observe foci of haematopoiesis [1, 3, 4, 7].Despite the presence of atypical cells with mitoses and nuclear polymorphism, chorangioma never undergo malignant transformation.

Chorangiomas 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 imaging can facilitate the diagnosis as the imaging makes the characteristic blood flow within the tumor apparent (Fig. 2). Magnetic resonance imagining may also play an important role in the detection this kind of lesion [5]. Placental chorangioma 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. On the basis of the blood flow within the mass, color Doppler imaging is considered to be a good sonographic marker and therefore, it can be used to differentiate vascular tumor from hematoma [4].

From the clinical point of view, only large chorangiomas are significant as their presence may lead to the development of a number of feto-maternal complications including fetal cardiomegaly, fetal anemia and thrombocytopenia, polyhydramnios, nonimmune hydrops, fetal heart failure, fetal growth restriction, preterm delivery, and maternal preeclampsia [1, 2].
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Fig. 3. Photograph of the 34-weeks placenta with the chorangioma

Fig. 4. Mature placenta with a stemmed chorangioma on its edge with conspicuous blood vessels

In 30% of the pregnancies with a large lesion, intrauterine fetal death takes place. The main problem for the developing fetus is a hyperdynamic circulation caused by the fact that the fetus has to supply blood to the large neoplasm which can cause hypoxia or malnutrition of the fetus. The pathophysiologic effect of an arteriovenous fistula in the systemic circulation results in lower fetal cardiac afterload, which in turn triggers hemodynamic compensations 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 [5]. For this reason, in all cases large chorangioma the clinician should focus on the assessment of cardiothoracic area ratio to exclude or confirm symptoms of cardiomegaly and cardiac insufficiency.

The possible pathophysiological mechanism for fetal anemia has been described as being related to fetomaternal hemorrhage, microangiopathic hemolysis or hemodilution [5, 8]. Similar mechanisms could also be responsible for the occurrence of the thrombocytopenia [8]. 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 [3, 5].

The most common complication of chorangioma is polyhydramnios, occurring in 14-28% of cases. The mechanism of the development of polyhydramnios is not clear. Several theories have been suggested. Firstly, polyhydramnios may be related to increased urine production due to the fetal hyperdynamic circulation, fetal heart failure or water imbalance. Another possible mechanism is linked to the localization of the tumor in close proximity of the umbilical cord insertion, which may constitute a mechanical obstacle to the blood flow and, as a result, it may cause transudation of fluid into amniotic cavity from tumor surface [9]. Some researchers claim that fetal hypoxemia can stimulate excretion of metabolites and this in turn, may raise the osmotic pressure of amniotic fluid and, in consequence, increase the production of fluid [9]. It is considered that all these mechanisms play a role in the development of polyhydramnios.

Various investigators have reported many other complications associated with chorangioma such as: preterm labour, antepartum bleeding, preeclampsia and congenital anomalies in the fetus. Antepartum bleeding is connected with the presence of placenta previa and abruption placentae, which are frequent in this group. Basing on the literature, every intrauterine fetal death was a consequence of the presence of a large chorangioma and of the developing fetal heart failure [2, 5]. The prematurity of the baby and the presence of diffuse an giomas in the placenta may also be responsible for intrauterine fetal demise [6].

In view of the well-known association between chorangiomas 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 no option. A number of treatment modalities have been discussed in the literature [5, 6, 10-12]. 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. 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 [6]. It must be stressed, however, that the procedures discussed do not treat the cause of the problem but only alleviate the symptoms.

More aggressive approaches, aimed at blocking vascular supply to the tumor, have been developed by several investigators. Quintero et al. [6, 10] suggested performing fetoscopic ligation and bipolar electrosurgery. Another option of management reported by Lau [11] is insertion of microcoils into the feeding arteries of chorangioma in order to induce thrombosis and devascularisation of the tumor. Finally, injection of absolute alcohol into the tumoral veins induced severe endothelial damage and intravascular coagulation, thereby devascularizing the neoplasm [12].

**Teratoma**

Placental teratomas are very rare. The most frequent localizations are: ovary, anterior mediastinum, retroperitoneum, presacral and coccygeal regions. Placenta, umbilical cord, pineal gland, skull, posterior mediastinum are uncommon sites of occurrence [1, 13]. Placenta is an extremely rare localization. Only 20 cases of the tumor have been described in the literature to date.

The pathogenesis of teratoma is probably connected with abnormal migration of totipotential embryonic germ cells from the dorsal wall of the yolk sac to the ovary. According to another theory, the tumors may derive from somatic or diploid embryonic germ cell [7, 13]. Teratoma may be develop from derivatives of all three germ cell layers. As a result, the tumor may be composed of different types of tissue such as: skin, hair, fat, muscles, cartilage, bone and vessels.

Teratomas of the placenta have an appearance of heterogeneous mass measuring from 2 to 7.5 cm. Most commonly they are located between chorion and amnion layer near the edge of placenta.

The teratoma of the umbilical cord has the same histological structure as placental teratoma. As a rule, this type of tumor occurs in the middle part of the umbilical cord. The largest teratoma described in literature was 9 cm in diameter.

The sonographic characteristics of the teratoma is based on the presence of tissue of varied echogenicity within the placental tumor or tumor attached to umbilical cord. Inside the lesion calcification foci as well as hyperechogenic foci without posterior acoustic shadowing may be observed. This is indicative of the presence of fat and fluid [13].

It is crucial to make prenatal diagnosis of placental teratoma. The neoplasm is benign and nearly always is associated with a normal outcome of pregnancy. The risk of pregnancy complications may correlate with the size of the tumor. A large teratoma can press on the vessels in umbilical cord leading to the development of thrombosis inside the vessels and eventually it may lead to hypoxia and death of the fetus [14, 15].

Placental teratoma and fetus acardius amorphous should be considered in the differential diagnosis. According to Fox et al. [16], fetus acardius amorphus has a separate umbilical cord and possesses some degree of polarity which makes it possible to identify its cranial and caudal ends. Such degrees of development do not exist in teratomas. However, some researchers believe that teratoma, represent an extreme form of fetus acardius amorphus [7, 13]. Partial or complete hydatidiform mole with coexisting fetus and hydropic degeneration of the placenta should also be taken into account in the differential diagnosis.

**Summary**

The significance of nonthrophoblastic placental tumor in the placental pathology still remains underestimated. Their relatively rare incidence, the asymptomatic course of development and lack of clinico-histological malignancy are the main reasons for neglect or small concern on the part of clinicians. In addition, the lack of routinely performed histological examination of the placenta may lead to overlooking small lesions located inside the tumor. Ultrasound examination with color Doppler flow imaging plays a crucial role in the detection of tumors of the placenta, which is essential considering the possibility of occurrence of serious feto-maternal complications. If a tumor is discovered, however, special attention should be paid to the examination of the fetal heart and specifically to the detection of early signs of congestive heart failure like: cardiomegaly, tricuspid value.
regurgitation. Moreover, in detection of fetal anemia, peak systolic velocity of the middle cerebral artery (MCA-PSV) corresponding to multiple of the median of the expected value, should be assessed. In case progressive polyhydramnios or signs of fetal cardiac failure are observed, clinical intervention seems mandatory to prevent fetal hypoxia or even demise. Consequently, persistent observation of these complicated pregnancies is necessary because of the discernible risk.

References


