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Can ultrasound be helpful in selecting optimal management methods for pregnancies complicated by placental non-trophpblastic tumors?

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Abstract

Placental chorioangioma is the most common subtype of non-trophoblastic placental tumors. Other subtypes are very rare and usually associated with an uneventful course of pregnancy. Most chorioangiomas are small and of no clinical significance. Giant chorioangiomas may be associated with serious fetal and maternal complications. So far, no established ultrasound guidelines are available for the management of placental non-trophoblastic tumors. This may be attributed to the rarity of the disease entity and its different clinical features and complications. In this article, the role of ultrasound findings such as the tumor's size, vascularity, feeding vessels, amniotic fluid and location of the placenta in the diagnosis, treatment and follow up of these tumors is presented relying on up-to-date literature review. Conservative management with serial ultrasound examinations can be an adequate method for monitoring small uncomplicated tumors. Ultrasound-guided procedures such as amnioreduction and cordocentesis can be used for amelioration of complications. Chorioangioma-specific treatment is reserved for complicated cases in the second trimester of pregnancy when prematurity is a matter of concern. Endoscopic laser ablation is indicated when the feeding vessel is superficial and small. Interstitial laser ablation is helpful when the placenta is located in the anterior uterine wall. Ligation of the feeding vessels is preferred when they are large. Alcohol injection should be performed away from the vasculature to prevent toxicity. Microcoils should be inserted as near as possible to the tumor to prevent collateral formation. Ultrasound is also a method of choice for monitoring the effectiveness of these procedures.

Placental chorioangiomas

Non-trophoblastic tumors are the most common neoplasms of the placenta. They include chorioangioma, teratoma, leiomyoma and hepatocellular adenoma[1–3]. Chorioangioma is the most common subtype. It was first described by Clarke in 1798[1]. Marchetti described three subtypes of placental chorioangioma: angiomatous (capillary), cellular and degenerative[4]. Capillary chorioangioma is the most common histological type[5] (Fig. 1). Most chorioangiomas are small and of no significant importance. Complications are mostly associated with chorioangiomas larger than 4 cm in diameter i.e. giant chorioangioma[6,7]. Giant chorioangiomas can cause polyhydramnios, intrauterine growth restriction (IUGR), placental insufficiency, fetal anemia, non-immunologic hydrop fetalis (NIHF) and intrauterine death[8–10]. Due to the rarity of the disease, most of the evidence about the management of giant placental chorioangioma is based on case reports in literature. In the largest retrospective study of 22439 placentas, the incidence rate was 0.61% of pregnancies[11]. The incidence rate of giant chorioangioma is rarer and ranges between 1/3500 and 1/9000[7]. Asokan *et al*. reported in 1978 for the first time antenatal diagnosis of placental chorioangioma by ultrasound[12]. Ultrasound is the gold standard for prenatal diagnosis and monitoring of placental chorioangiomas[13]. However, at the moment there is no single clinical protocol that may help the physician to choose the most appropriate method of treatment of these tumors. The aim of this review study is to summarize the ultrasound findings of these tumors and their complications. The use of certain ultrasound features will be discussed for selecting the most appropriate invasive or non-invasive method of management.

Gray-scale ultrasound features of placental chorioangioma

Chorioangioma usually presents as a single nodule in the fetal surface of the placenta near the insertion of the umbilical cord[14] (Fig. 2). Multiple placental chorioangiomas are rarer[15]. Hyperechogenic areas suggesting hemorrhage as well as calcification can be seen. The tumor may contain several thin septa[16]. The echo pattern of chorioangioma is stable[1]. The borders of the chorioangioma are well defined[17]. The dimensions of the chorioangioma may increase during pregnancy or remain the same[8–18]. Chorioangioma can be overlooked on ultrasound examination even if the tumor is large[6]. Prenatal diagnosis can also be an incidental finding during a routine ultrasound examination[19]. The size may reach several centimeters[20]. Chorioangiomas are found more often in multiple pregnancies. They are associated with female gender of the fetus in 72% of cases[11].

Doppler ultrasound assessment of placental chorioangioma

Doppler ultrasound is the gold standard for diagnosis of placental chorioangioma[21]. Substantial vascularity indicates the angiomatous type of chorioangioma[22] (Fig. 3).

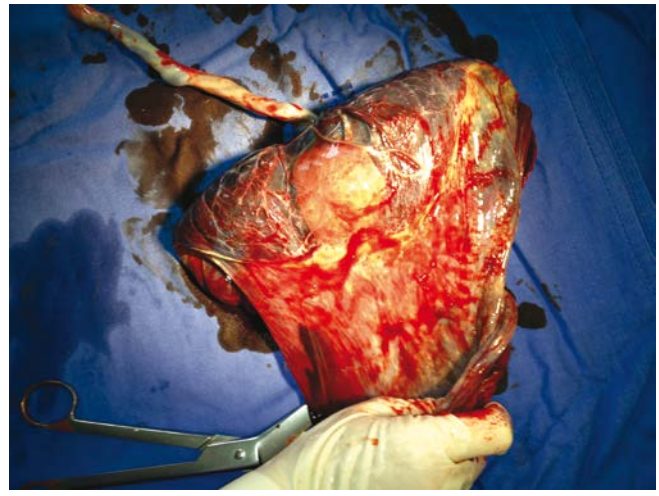

Fig. 1. *Macroscopic appearance of marginal placental chorioangioma*

Diagnostic difficulties may arise with cellular and degenerative subtypes of chorioangioma where the vascularization is less evident[23]. Blood vessels of chorioangioma are derived from the fetal circulation, so the feeding vessels have the same pulsatile flow of the umbilical artery. The low resistance of the feeding vessels is related to the arteriovenous shunt[1]. The vascularity of chorioangioma is one of the prognostic factors for the course of pregnancy. Unvascularized chorioangiomas tend to be unrelated to complications, while vascularized tumors can predispose to typical complications of chorioangioma[24,25].

Ultrasound assessment of the fetus

Measurement of fetal biometry and estimated fetal weight is indicated, as chorioangioma is associated with IUGR[1]. IUGR can be related to placental inefficiency related to decreased area of placental tissues required for adequate exchange of nutrients[17]. Arteriovenous shunt of the blood

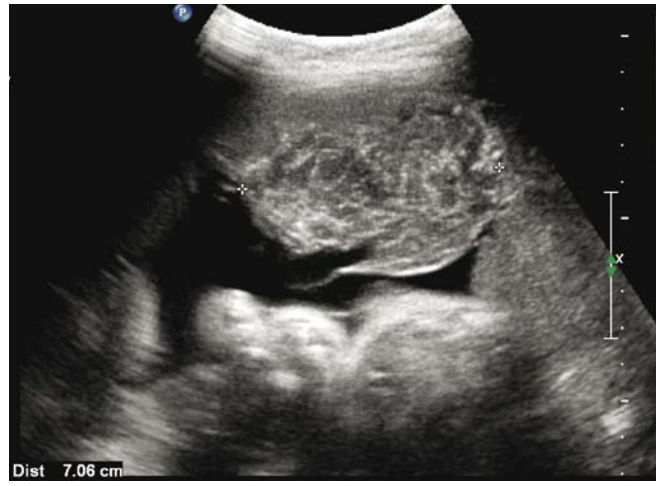

Fig. 2. *Gray-scale ultrasound of giant placental chorioangioma. The diameter of the tumor is 70 mm*

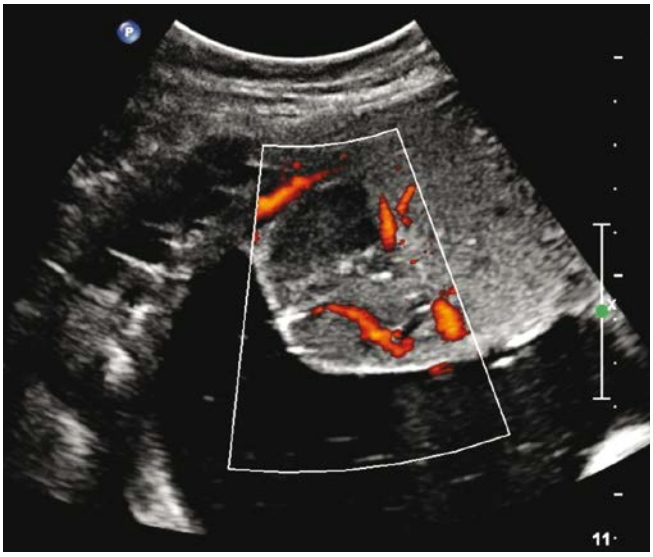

Fig. 3. *Power Doppler ultrasound of placental chorioangioma showing the vascularity of the mass*

and fetal hypoxia caused by unoxygenated blood that bypasses the maternal circulation through chorioangioma can cause high cardiac output and secondary fetal cardiomegaly[26]. Ultrasound features of heart failure include enlargement of the heart, decreased contractility and pericardial effusion, increased cardiothoracic ratio and developing fetal hydrops[8,27]. Coincidental presence of congenital anomalies with placental chorioangioma have been reported[28]. Assessment of the middle cerebral artery peak systolic velocity MCA-PSV is useful for detecting fetal anemia and high cardiac output failure[26]. Not always MCA-PSV reflects the severity of fetal anemia. Hellmund *et al*. reported a masked fetal anemia caused by severe bilateral hydrothorax which led do decreased ventricular filling, stroke volume and cardiac output resulting in false decreased MCA-PSV. Drainage of the hydrothorax by bilateral thoraco-amniotic shunts resulted in reversal of the pathological events revealing true high MCA-PSA[29]. Figure 4 shows the increased multiple of medians (MoM) of MCA-PSV as a complication of chorioangioma. Assessment of Doppler flow of umbilical vessels and middle cerebral artery is used for the evaluation of the wellbeing of the fetus[8,22,30].

Ultrasound assessment of the remaining placenta, umbilical cord and amniotic fluid

Placentomegaly has an ultrasound association with NIHF caused by chorioangioma[29]. Polyhydramnios is the most common complication of placental chorioangioma occurring in 18–35% of cases of giant chorioangiomas[30]. Possible transudation of fluid from the vessels together with placental deficiency are responsible for polyhydramnios[22]. Hyperdynamic circulation can cause an increased glomerular filtration rate and urine production[25]. Polyhydramnios, characterized by excess of amniotic fluid, can be assessed using the single deepest vertical pocket (DVP) or amniotic fluid index (AFI). Polyhydramnios can be classified as mild, moderate or severe, when the DVP has a value of 8–11 cm, 12–15 cm and above 16 cm respectively. This parameter is simple, and can be a method of choice for multiple gestation. AFI Values of 25–30 cm, 30.1–35 cm, and =>35.1 cm indicate mild, moderate and severe polyhydramnios respectively[31]. Figure 5 shows mild polyhydramnios caused by giant chorioangioma. A single umbilical artery and velamentous insertion of the umbilical cord have a recognized association with chorioangiomas[30] (Fig. 6).

Three dimensional ultrasound imaging of chorioangioma

In three dimensional (3D) ultrasound the surface of chorioangioma is rough and thick[32]. Shih *et al*. reported

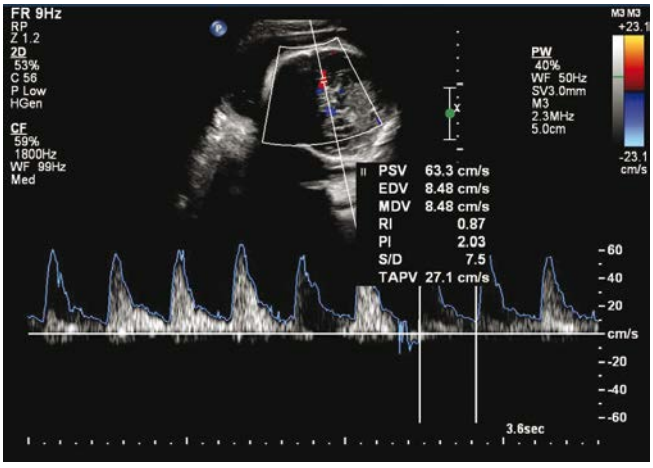

Fig. 4. *Assessment of MCA-PSV as an indirect method of detecting fetal anemia and heart failure. The MCA-PSV in this patient at 28th week of gestation corresponds to 1.7 MoM*

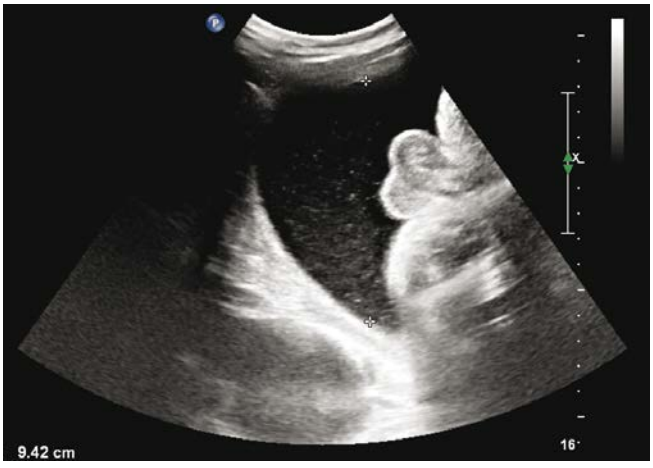

Fig. 5. *Maximum pocket volume of 9.4 cm indicating mild polyhydramnios*

the use of 3D power Doppler ultrasound for the diagnosis and monitoring of giant chorioangioma. The authors could display the angioarchitecture of the tumor, confirming the fetal source of blood supply to the tumor. This method can show the volume of the mass, as well as the vascularity index (VI) of the tumor[16]. There is a lack of evidence in the literature that 3D ultrasound is superior to two dimensional type for the management of chorioangioma.

Ultrasound of maternal pelvis, abdomen and breast

Ultrasound assessment of maternal organs to detect metastases is not indicated, since chorioangioma has no malignant potential[1]. However, the definitive diagnosis of the tumor can only be established by histological examination. If the diagnosis is doubtful, especially for patients with suspected or confirmed malignant disease, imaging diagnostics for the mother is indicated since metastases to the placenta and transplacental transfer of the neoplastic disease to the fetus have been reported[33]. If the diagnosis of chorioangioma is confirmed after delivery, maternal follow-up with ultrasound is not needed[22].

Role of ultrasound in monitoring placental chorioangioma

There is no specific protocol for monitoring asymptomatic or symptomatic placental chorioangioma. Planned delivery is the method of choice for term pregnancies complicated by chorioangiomas. When the pregnancy is not in term, other methods of treatment should be considered to prevent prematurity and reduce complications[5]. The monitoring frequency depends on the size of chorioangioma, trimester of the pregnancy and associated complications. Physicians may consider 3–4-week intervals for small chorioangiomas, while larger tumors should be monitored every 1–2 weeks[17]. 3D power Doppler can show decrease of the vascularization. Decreased VI with simultaneous increase of the size of the chorioangioma may reflect the hemodynamic changes caused by simultaneous infarction of the tumor[16].

Ultrasound-guided procedures for amelioration of symptoms caused by placental chorioangioma

Ultrasound-guided therapeutic amniocentesis is used for reduction of the amount of the amniotic fluid, thereby decreasing maternal discomfort and possible complications of polyhydramnios, such as premature threatened labor[1,22]. Amnioreduction can be repeated in pregnancy[22]. Ultrasound-guided cordocentesis is indicated to confirm fetal anemia, and to transfuse blood to the fetus to correct it[5].

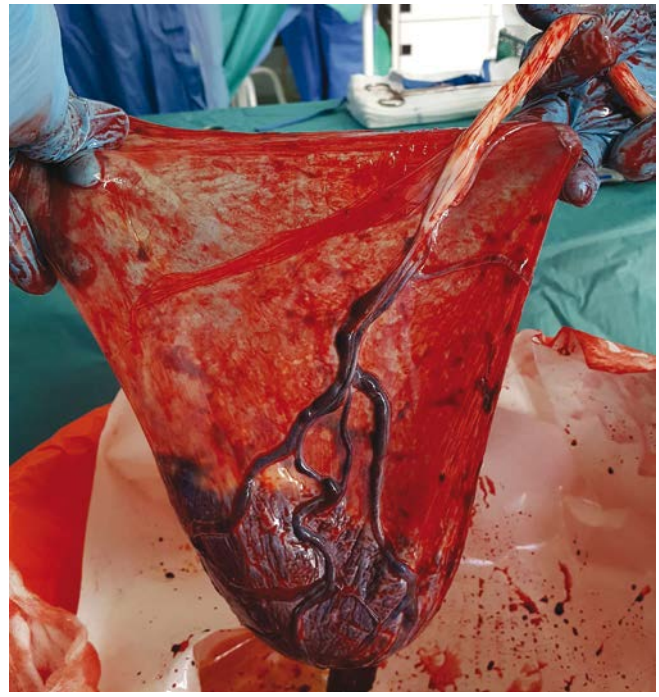

Fig. 6. *Velamentous insertion of the umbilical cord*

Ultrasound-guided procedures used for specific treatment of placental chorioangioma

Definite prenatal treatment of placental chorioangioma should be reserved for cases with life-threatening complications, such as NIHF, or when prematurity is a matter of concern[8]. Doppler ultrasound can help to choose the most appropriate procedure depending on the localization of the placenta and vascular assessment of the tumor and the feeding vessel, its size and distance from the umbilical cord[5]. Several methods have been described in literature for chorioangioma-specific treatment. These include laser ablation, alcohol injection, insertion of microcoils, and ligation of blood vessels[23,25,34–37]. Fetoscopic laser ablation seems to be the method of choice for cases where the feeding vessels are small and superficial[21]. When the feeding vessel of chorioangioma is a secondary branch from the umbilical artery, laser photocoagulation can be performed without a theoretical risk of placental insufficiency, since the umbilical artery does not end in the tumor but continues to the remaining placenta[8]. Interstitial laser ablation might be a choice for cases where the placenta is located on the anterior wall, where endoscopic ablation can be technically difficult[35]. Laser ablation may not be suitable for a large feeding vessel, as it may rupture during the procedure[34]. It is also not applicable when the feeding vessel is deep or when it is near the insertion of the umbilical cord because of a risk of injury to the viable placenta[23]. Quintero *et al.* suggested ligation of the arterial supply after subchorionic dissection as a choice for larger vessels, because of a higher risk of rupture during laser ablation[37]. Ercan *et al.* reported ultrasound-guided injection of alcohol directly into the tumor to treat chorioangioma.

Knowledge of the angioarchitecture of the tumor is essential, as alcohol should be injected into the center of chorioangioma, away from the vascular structures[25]. In case of microcoil insertion, caution should be exercised to insert as near as possible to the tumor to minimize collateral formation. The technique has no risk of distal embolization of the fetal circulation[36]. Embolization of the feeding vessels has no risk of fetal toxicity, and can be a method of treatment of chorioangioma[5].

Use of ultrasound to monitor the effect of treatment of chorioangioma

Ultrasound examination can be used for monitoring the effect of the procedures used for the management of chorioangioma or its complications. Ultrasound can be used for detecting the remaining amniotic fluid index after amnioreduction[22]. Doppler ultrasound is used for evaluation of the blood flow in the feeding vessels and tumor itself. It can show the effectiveness of the procedure by showing the absent or decreased blood flow in the feeding vessels and the tumor[25,27]. The mass may decrease in size, and can develop cystic appearance. Reversal of features of NIHF can also be detected[8]. Ultrasound is necessary for assessing fetal wellbeing and viability since sudden fetal death after surgical interventions have been reported[34,37]. Mendez-Figueroa *et al*. reported paradoxical unexpected development of severe NIHF after amnioreduction for chorioangioma-induced polyhdramnios. The authors suggested that amnioreduction should be performed after laser ablation[34]. Increased tumor bed blood flow or direct hemorrhage to the tumor due to sudden decrease of intrauterine pressure may explain the ''steal'' phenomenon[8].

Other non-trophoblastic placental tumors

Placental teratomas are very rare and were described for the first time by Morvilli in 1925[38]. They are composed of derivatives of all three germ layers[2]. They resemble fetus amorphous, but lack the umbilical cord and central skeletal formation of this condition[38]. Ultrasound features are that of a heteroechogeneous mass. Echogenic foci with acoustic shadows represent calcification. Hyperechoic foci without acoustic shadows suggest fat[2]. Placental teratomas are nearly always associated with a normal pregnancy outcome. Large teratomas can press umbilical vessels leading to the vessels' thrombosis[39].

Few cases of placental leiomyoma have been reported in literature. Placental leiomyoma may appear as submucous myoma in the first trimester[40] and has an appearance of a hypoechoic lesion. Some authors suggest that pedunculated uterine leiomyomas are incorporated into the placenta during its development. Characteristic fetal or maternal waveform by color Doppler may indicate the possibility of myoma existence[3]. Placental leiomyoma may be overlooked during routine ultrasound examinations[40].

Hepatocellular adenoma of the placenta is an extremely rare tumor. It remains inconclusive whether this lesion represents a neoplasm rather than a rare ectopic or heterotopic occurrence[41]. It is usually described as a solitary tumor like a nodule, involving the placental parenchyma. It is usually an incidental finding without a significant pathological impact[42].

Differential diagnosis of placental tumors

Although chorioangioma is the most common type of non-trophoblastic placental tumors, ultrasound detection of placental tumors should consider other pathological conditions in the differential diagnosis. Chorangiocarcinoma, a complex lesion characterized by torophoblastic proliferation within chorioangioma, has similar ultrasound features to chorioangioma. Few cases of chorangiocarcinoma have been reported in literature. In all of the reported cases no malignant metastases were reported[43]. Confirmation of continuity of feeding vessels with the fetal circulation by Doppler ultrasound can exclude other pathological conditions like placental hemorrhage, maternal lakes, or degenerated myoma[16]. In 3D ultrasound the walls of a placental cyst or subchorionic hematoma are transparent-like structures, and the internal texture can be clearly identified[32]. The echo pattern of blood clots, as opposed to chorioangioma, changes with time. A partial mole has a diffuse pattern. Uterine myoma can be seen in the maternal surface. Chorioangioma can be confused with placental teratoma. The vascularity of chorioangioma can differentiate it from teratoma[1]. Calcification is more characteristic for teratoma[44]. Chorioangioma should be differentiated from secondary metastases to the placenta. Malignant melanoma is the most common neoplasm metastasizing to placenta during pregnancy[33]. Ultrasound findings include focal lesions with altered echogenicity relative to that of a normal placenta[44].

Summary

No precise management guidelines for the management of placental non-trophoblastic tumors have been developed so far. The lack of guidelines can be related to the rarity of this disease entity and the diversity of its clinical features. Treatment modalities for chorioangioma are mostly experimental. A systematic literature review of chorioangioma may help in establishing a consensus for choosing the best method of management[8]. Interpretation of ultrasound findings should be carried out with caution, as normal findings in the ultrasound do not rule out severe complications[29]. On the other hand, ultrasound imaging of giant chorioangioma does not necessarily indicate the presence of fetal and/or maternal complications[14]. Placental chorioangioma, even if rare, should be considered in the differential diagnosis, and looked for carefully when complications typical for this tumor, like polyhydramnios and NIHF, are present[6]. The management of each case of chorioangioma

is individual, depending on many factors. Ultrasound can detect multiple abnormalities at the same time, and the sequence of certain procedures should be considered with caution, e.g. amnioreduction after laser ablation[34]. An ultrasound diagnosis of chorioangioma is only suggestive, and the final diagnosis is established upon histological examination of the tumor, which might be a malignant neoplasm as well[44]. Other non-trophoblastic placental tumors are rare, and usually not related to pregnancy complications[39].

Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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