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Review Article

PLACENTA & INTRAUTERINE FETAL DEATH

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ABSTRACT

Placenta has a significant role in etiopathology of fetal death. About 11.6% cases of fetal death are due to placental pathology. CORM system of fetal death classification has reduced the unclassified category to 8.5%. Maternal vascular malperfusion, fetal vascular thrombosis, umbilical cord pathologies contribute a lots. Understanding these pathologies can help us to manage the subsequent pregnancies by evaluation of maternal cardiovascular status, diabetes & thrombophilia screening, prophylactic aspirin, early delivery etc.

Key words: fetal, malperfusion, pathology, stillbirth, vascular

INTRODUCTION

Causal relationship between fetal death and placental pathology has traditionally been given less importance. The placenta is the gateway between mother and the fetus. It supplies essential nutrients to the growing fetus, and also provides a protective environment. Fetal nutrition depends on the vascular tree of the placenta, which is continuously growing and developing as the gestation advances. Whenever any external threat comes an inflammatory response against that happened (placental protective function). Such responses may occur at feto-maternal junction where organisms may enter the placental environment whilst fetal antigens may be presented to the maternal immune system allowing a response leading to the release of mediators of inflammation.[1]

Histopathological examination of the placenta is to be done to determine the cause of stillbirth/fetal death.[2] Placental examination alongwith autopsy of the fetus can give a good highlights towards the etiology of fetal death.[3] Routine examination of placenta at birth and genetic studies in suspicious cases will enable us to counsel the parents about the possibility of recurrence of fetal death or congenital abnormality.[4] Placental pathology contributing to fetal death is 11.6%.[5]

FETAL DEATH CLASSIFICATION SYSTEM

A new fetal death classification system [CORM system {CondiciÓn Obstétrica Relevante de la Muerte (Spanish) (relevant obstetric death condition)}][5] based on obstetrical history and placental biopsy is been developed in Chile. The histopathological evaluation of placenta revealed the damage that occurs to placenta as a consequence of original obstetric condition, ultimately leading to fetal death. The causes are been classified under the following headings –

1) Maternal conditions
2) Fetal conditions
3) Placental conditions
4) Uterine conditions
5) Asphyxia during labor
6) Conditions not classifiable

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The placental pathologies are been categorized as –

1. *DPPNI* {Desprendimiento Prematuro de Placenta Normo Inserta (Spanish)}: Separation of the placenta from the uterus, in the absence of maternal-fetal pathology and with placental lesions: hematoma and retroplacental hemorrhage, subcorial hemorrhage, villous infarcts, intervilliary thrombosis
2. *Maternal and fetal circulatory disorders and IUGR*: Absence of maternal-fetal pathology, with IUGR, with or without DPPNI, with placental lesions: thrombotic fetal arteriopathy, intervillary and fetal arterial thrombosis, increased deposit of perivellosiary fibrinoid, villous infarcts, hematoma and retroplacental hemorrhage
3. *Deciduitis, chronic vellosistis and IUGR*: Absence of maternal-fetal pathology, with IUGR and placental lesions: chronic lymphoplasmacytic deciduitis, chronic chorioamnionitis, perivellositis and chronic vellositis, intervilliary thrombosis
4. *Other and IUGR*: Absence of maternal-fetal pathology, with IUGR and with placental lesions: villous edema, corangiosis.
5. *Pathology of the umbilical cord*: Circular knot, with thrombosis and / or rupture, cord hyper-rotation, procidentia/prolapse, hematoma, velamentous insertion

The advantage of this classification system is that the non-classifiable or non-explainable condition is only 8.5%. For more detailed information refer to the original article @ reference no 5.

Most frequently encountered primary placental conditions responsible for fetal death are abruptio placentae (5.3-12.9%) followed by placental insufficiency (2.6-8.1%) and placenta praevia (1.7%).[2,6] Placental insufficiency is considered when infarction of "about 25% placental mass" has occurred,[7] though it is described as ">30% parenchymal loss" in another study.[8] Pathology of placenta responsible for fetal death are chorioamnionitis, cord abnormalities, delayed villous maturation (DVM), fetal thrombotic vasculopathy (FTV), hemorrhagic endovasculitis (HEV), villitis of unknown aetiology (VUE).[2]

VASCULAR PATHOLOGY

Maternal vascular underperfusion – due to inadequate spiral artery remodeling or pathology of spiral artery (decidual vasculopathy). Commonly seen in case of PIH. The parenchymal pathology seen are placental hypoplasia, increased syncytial knots, villous agglutination, increased perivillous fibrin, distal villous hypoplasia, abnormal villous maturity, infarction, retroplacental hematoma.[9]

Fetal thrombotic vasculopathy – Thrombosis in the umbilical cord, chorionic plate or stem villus vessels (recent or remote) and / or secondary degenerative pathology in the fetal vasculature by thrombotic obliterated vessels (e.g. avascular chorionic villi). Pathologies seen are hemorrhagic endovasculopathy, intimal fibrin cushions, fibromuscular hypertrophy, villous stromal-vascular karyorrhexis.[9]

Massive perivillous fibrin deposition (MFD) on placenta has a deleterious effect on pregnancy. Severe cases (MFD extended over more than 50% of the placenta) are more often associated with fetal death and abnormal umbilical artery Doppler velocimetry in compare to moderate cases (MFD extended over between 25% and 50% of placenta).[10]

FETAL GROWTH RESTRICTION (FGR)

In FGR, fetal death has increased syncytial nuclear aggregates (SNAs) & trophoblast area and reduced proliferation & villous vascularity. Applying quantitative assessment in addition to qualitative assessment may help us to reduce the proportion of unexplained fetal death.[11] Low weight placenta and oligohydramnios are found in early fetal death.[12] Placental pathology due to maternal vascular underperfusion is the main contributor of fetal death (34-38)% which is most prominent during preterm period, in PIH, and declining after that. At term gestation, fetal death is mostly due to developmental pathology of placental parenchyma.[9]

In search of placental pathology responsible for fetal death and fetal growth abnormalities among 319 singleton stillbirths and 1119 singleton live births at ≥24 weeks, 25 suspected placentas were investigated. Out of these 25, 15 placentas were significantly associated with fetal death. Ten of the 15 were also associated with fetal growth abnormalities (single umbilical artery; velamentous insertion; terminal villous immaturity; retroplacental hematoma; parenchymal infarction; intraparenchymal thrombus; avascular villi; placental edema; placental weight; ratio birth weight/placental weight) while 5 of the 15 associated with fetal death were not associated with fetal growth abnormalities (acute chorioamnionitis of placental membranes; acute chorioamionitis of chorionic plate; chorionic plate vascular degenerative changes; perivillous, intervillous fibrin, fibrinoid deposition; fetal vascular thrombi in the chorionic plate).[13] A diagnostic challenge sometimes encountered in cases with prior intrauterine fetal death, since degenerative changes post demise result

in a similar histomorphologic picture. The diffuse versus focal nature of the lesions may help in the distinction.[14]

LARGE FOR GESTATIONAL AGE

In case of large –for-gestational age (LGA) fetuses, the causes of fetal death are grouped as fetal (43.5%), placental (22.6%), and maternal (11.2%). Among placental causes abruption and infarct are most common and this is more common in diabetic mothers (33% vs 18% in the entire LGA group). Most fetal death in diabetic mothers occurs after 28 weeks.[15]

Regarding intrapartum fetal death, except in cases of intrauterine infection, placental vascular abnormalities are unlikely to be associated with intrapartum asphyxia leading to fetal death during labor.[16]

UNEXPLAINED FETAL DEATH

The risk of unexplained fetal death increases late in pregnancy – aging of the placenta may play a role. Aging causes oxidative damage to DNA, RNA, and lipids. There is a role for aldehyde oxidase 1 and G-protein-coupled estrogen receptor 1 in mediating placental aging that may contribute to stillbirth.[17] In unexplained stillbirth, there is an association between elevated amniotic fluid chemokine ligand (CXCL)10 and chronic placental inflammatory lesions. An elevated amniotic fluid CXCL10 concentration (above the 95th centile) was present in 60% of the cases, and a receiver operating characteristics (ROC)-derived cut-off of 2.9 ng/mL had a sensitivity of 73% and a specificity of 75% in the identification of chronic placental inflammatory lesions.[18]

COMMON UNDERLYING PLACENTAL CAUSES[19]

1) **Preterm fetal death:** Global/partial maternal vascular malperfusion (accelerated maturation), global/partial fetal vascular malperfusion (umbilical cord accident), abruptio placenta
2) **Term fetal death:** Abruptio placenta, global/partial fetal vascular malperfusion (umbilical cord accident), fetomaternal hemorrhage, delayed villous maturation

MANAGEMENT IMPLICATIONS[19]

Knowledge of the placental pathology and their possible consequences will help the obstetricians to tackle the situation in better way. Some of the pathologies are due to the vascular malperfusion of the maternal aspect of the placenta whereas some are due to the vascular malperfusion of the fetal aspect of the placenta.

1) Severe global/partial maternal vascular malperfusion:
   Evaluation of maternal cardiovascular status, glucose tolerance test, thrombophilia, renal function; uterine artery Doppler, early third trimester placental ultrasonography
   Treatment options - weight loss, aspirin therapy, early delivery in subsequent pregnancies
2) Complete/segmental fetal vascular malperfusion
   Maternal thrombophilia workup, diabetes screening, platelet count

Placental examination alongwith fetal autopsy can bring more information regarding the cause –effect relationship of placenta in causing intrauterine fetal death. However fetal autopsy is less performed in many instances due to parental refusal.20 Proper passionate counseling and public awareness programme may change the scenario and help in realizing the etio-pathology so as to research for more avenues for prevention fetal death.

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