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Placenta: chronicle of intrauterine growth restriction

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Abstract

The foundation for adult health is laid *in utero* and requires a healthy placenta. A common manifestation of abnormal placental development is impaired fetal growth. While placental pathology is the final common denominator in many cases of fetal growth restriction, a variety of discreet lesions have been described involving both the maternal and fetal circulations at their confluence in the placenta. Detailed examination of the placenta provides a means of elucidating the pathophysiology of poor fetal growth. This is an essential step in developing effective strategies for the prediction, prevention, and possible treatment of the growth restricted fetus.

Introduction and context

More than merely a conduit for the provision of oxygen and nutrients to the fetus, the placenta actively regulates the passage of substrates necessary for fetal growth and development. In particular, amino acids are critical as they are precursors for the protein synthesis necessary for growth. The appropriate balance and quantity of amino acids is essential for fetal and placental health. Provision of amino acids from the maternal circulation into and through the placenta requires the coordinated activity of multiple transport proteins, which function differentially in the microvillus membrane and basal membrane to provide and maintain the levels of specific amino acids necessary for normal fetal growth [1]. Intrauterine growth restriction (IUGR) connotes failure of the fetus to achieve its growth potential [2]. While genetic abnormalities and chronic fetal infections may cause IUGR, most cases result from placental pathology [3]. Both *in vitro* and *in vivo* studies have demonstrated reduced volume and transport capacity for amino acids in the placentas of IUGR versus 'appropriate for gestational age' fetuses [4,5].

The consequences of aberrant fetal growth secondary to placental dysfunction extend far beyond the intrauterine phase of our existence. A variety of adult chronic illnesses, including cardiovascular disease, dyslipidemia, type II diabetes, and obesity, are now felt to be a manifestation of fetal malnutrition [6], usually resulting from placental changes precluding optimum function. The finding that the placenta is capable of influencing an individual's general health years following its relatively brief service is a testament to its critical effect on intra- as well as extra-uterine survival. Growth of the placenta, its blood vessels, and its blood supply are intertwined such that, under normal circumstances, fetoplacental growth correlates with the ability to provide oxygen and nutrients to the placenta for subsequent transfer to the fetus. As the intermediary between the mother and fetus, the placenta is uniquely qualified to support fetal growth but also uniquely susceptible to abnormalities affecting the maternal and fetal vascular trees. Despite the intuitive importance of placental dysmorphology in fetal growth disorders, a systematic approach to the description of placental changes has been lacking [7].

Recent advances

An approach to the categorization of placental injury associated with IUGR has been proposed as follows: (a) lesions of maternal underperfusion, including decidual vasculopathy, infarcts, distal villous hypoplasia, increased syncytial knots, and intervillous fibrin disposition [8]; (b) fetal vascular obstructive lesions, including large fetal

vessel thrombi, avascular villi, and chronic villitis with obstructive fetal vasculopathy – these changes are the sequelae of circulatory stasis, vascular injury, and coagulopathies [9]; (c) lesions causing reduced placental reserve, such as extensive perivillous fibrin deposition and extensive chronic villitis [7]; (d) dysmorphic villous changes, including villous edema, villous immaturity, and villous maturation defects characterized by enlarged dysmorphic villi and capillary vessels surrounded by edematous stroma [10].

The final common pathway for all of these disturbances of normal placental anatomy is that they render the placenta incapable of normal nutrient and gas exchange in the affected areas. Progression of these changes can result in chronic undernutrition and fetal growth restriction. Of the placental lesions associated with IUGR, the most common are those of maternal underperfusion [10,11]. Decidual vasculopathy refers to a variety of pathologic changes in the spiral arteries of the decidua that result in diminished flow through these vessels. Since the spiral arteries supply oxygen and nutrients to the intervillous space for subsequent transfer to the fetus, conditions that interfere with the normal adaptation and perfusion of these vessels may ultimately impair placental and fetal growth. Normal placental development is characterized by remodeling of the spiral arteries. This refers to the process whereby trophoblastic cells invade and replace the normal muscular intimal lining of the vessel walls, resulting in fixed dilation that promotes blood flow to the placenta [2]. Acute atherosis, the most common form of decidual vasculopathy, is characterized by fibrinoid necrosis of the vessel wall and represents failed conversion of the spiral arteries. Hypoplasia of the terminal villi is also a feature of early onset circulatory abnormalities. Such insults are secondary to abnormal trophoblast infiltration and implantation. These abnormalities can occur early in pregnancy, meaning that these placentas are destined to underachieve, often with demonstrable effects on fetal growth. The most common maternal conditions associated with decidual vasculopathy include hypertensive disorders (chronic hypertension and pre-eclampsia) and antiphospholipid syndrome. Other factors implicated in maldevelopment of the uteroplacental vascular connection include inherited thrombophilias and type I diabetes with vascular disease [3,12].

Implications for clinical practice

Fetal growth restriction is associated not only with perinatal morbidity and mortality, but with a predisposition to adult chronic illnesses. Normal placental growth and development is a prerequisite to normal fetal growth and development. While fetal vascular obstructive lesions and primary villous pathology, such as perivillous fibrin deposition and dysmorphic villous changes, may impair normal fetal growth, most cases of IUGR are secondary to abnormal placentation resulting from lesions of maternal underperfusion and compromised uteroplacental circulation. Women at especially high risk for these changes are those with hypertensive disorders. The pathology of both chronic hypertension and pre-eclampsia predispose to an ongoing process of placental vascular changes that compromise uteroplacental blood flow with detrimental effects on fetal growth and well being. Diligent examination of the placenta may provide the only opportunity to fully understand 'what went wrong' in cases of abnormal fetal growth [13].

Abbreviation

IUGR, intrauterine growth restriction.

Competing interests

The author declares that he has no competing interests.

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