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Review Article

The Marvellous Short –Lived Organ: The Placenta

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Abstract

Placenta is a transient organ that grows, differentiates and matures during a short life span. It starts to develop during implantation of the conceptus and is expelled shortly after labor. The placenta has nutritive, excretory, respiratory and immune functions, as well as hormonal production. The differences in placental structure between different mammals modulate the transfer of substances through placental barrier. Multiple placental variants have been encountered in medical practice. These variants may affect normal growth and/ or normal delivery of the baby. Correlation of basic knowledge about placental development, structure, comparative anatomy and function together with clinical findings is crucial for proper management in pregnancy and in medical research.

Introduction

Placenta is the organ shared between mother and her baby. It is the first connection between both. As the placenta is expelled after delivery of the fetus, it is also named after birth (together with the expelled fetal membranes). In Egypt, it is given a name which means (getting rid of), as relief from labor pains occurs after delivery of placenta. What happens to placenta after birth is a question which may be asked by us. In mammals (including humans in some cultures) mothers eat their placentas. In the rural areas of my country,

Egypt, placenta is buried in the ground or even in the family tombs. However, most of mothers do not know what happens to their placentas which actually thrown in the garbage of hospitals. Although placenta has multiple functions, still its main function is nourishment of the baby [1].

Development of the placenta

How is placenta formed? The answer of this question explains how the endometrium is transformed into decidua. A process called implantation must occur, thus the conceptus can attain the maternal blood supply. The onset of this process varies in different mammals. In mice, implantation occurs 4 days' post coitum, while in humans it happens after 9 days. Cows need up to 30 days after fertilisation for implantation to occur [2]. The implantation in humans and guinea pigs is characterized by invasion of the trophoblast through the uterine epithelium to become imbedded into the endometrium. This type is called interstitial implantation. In some mammals as hamsters, rats and mice, the implantation is eccentric where the uterine epithelium invaginates the trophoblast. However, in other mammals like sheep, the blastocyst grows to come into contact with the endometrium without penetration which is termed centric implantation. These variations would modulate the structure and function of the placenta [3].

The first step in the process of implantation is the adherence of the conceptus (blastocyst) to the endometrium. The blastocyst-endometrium interaction induces decidual reaction in which proliferation of the endometrial stromal cells results in morphologically different decidual cells. In addition, the endometrium becomes highly edematous with increased vasculature and the endometrial glands elongate extremely, become tortuous and secrete abundant glycogen and mucus [4].

An enzyme similar to trypsin enables the blastocyst from hatching from its outer cover, zona pellucida [5]. Soon after, the blastocyst expands and the cells of inner cell mass differentiate into two layers to form the bilaminar embryonic disc. The blastocyst-endometrium interaction is multifactorial. L selectin on the trophoblast cells enables the initial attachment of the blastocyst to the carbohydrate receptors on the endometrial epithelium. In addition, the trophoblast cells express integrins which interacts with laminin and fibronectin for further attachment and invasion of the blastocyst to the uterine wall [6].

Meanwhile, at the site of contact between blastocyst and endometrium the trophoblast differentiates into inner cytotrophoblast and outer syncytiotrophoblast [6]. Soon after, this outer syncytium will develop vacuoles which fuse together to form large lacunae. Cells from the syncytiotrophoblast creep through the endometrium and erode the maternal blood sinusoids. Accordingly, the maternal blood flows from maternal blood sinusoids to syncytial lacunae. Uteroplacental circulation is now established [7] (fig.1).

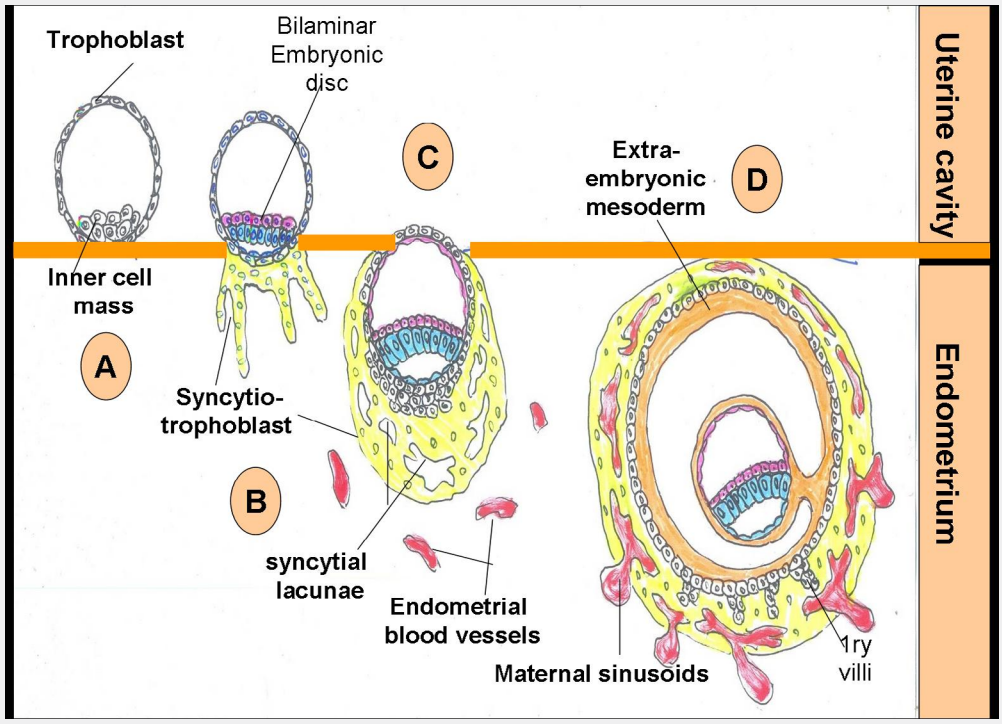

Figure. 1: *Implantation and development of placenta*

A) The blastocyst adheres to the endometrium.
B) The trophoblast differentiates to give syncytiotrophoblast which penetrates through the endometrium.
C) Multiple syncytial lacunae appear and the endometrial blood vessels become dilated.
D) The syncytial lacunae join the maternal blood sinusoids with establishment of utero-placental circulation. Notice the formation of the primary villi.

As implantation proceeds, the syncytiotrophoblast surrounds the whole blastocyst. Some cytotrophoblast cells penetrate through the syncytiotrophoblast to form the primary villi [6]. After complete implantation and formation of trilaminar embryonic disc, mesodermal invasion into the primary villi occur to be transformed into secondary villi. Then, some of those mesodermal cells differentiate into blood vessels for formation of the tertiary villi by the end of the third week of pregnancy [8].

During the next months, the existing stem villi give rise to multiple small extensions which protrude into the intervillous spaces as free villi. In human placenta, at the beginning of the 4th month, the fetal blood is only separated from the maternal blood by syncytium and endothelial wall of blood vessels (hemochorial pattern) [6].

Maturation of human placenta, placental grading and aging

The placenta grows dramatically from the third month of gestation until term. Deopa *et al.* [9] discussed placental maturation and grading according to ultrasonographic findings. They claimed that all placentas start with grade 0 in early pregnancy in which there is straight chorionic plate and homogenous placental substance. Three grades of maturation then can be demonstrated; grade 1 in which there is undulations of the chorionic plate with scattered ecogenic areas in the placental substance, grade II in which chorionic plate indentations extend into the placenta with linear densities and linear small areas in the basal layer and grade III in which chorionic plate indentations reach to the basal layer, the placental densities become circular and in basal layer become larger. Maturation and calcification of the placenta is a normal process as pregnancy progresses. Changes can start from the 12th week of pregnancy onwards. Normally, placenta can reach grade I around the weeks 31 to 32, grade II around 36-37 weeks and grade III around 38 weeks of pregnancy. A direct correlation exists between the growth of the placenta and the growth of the fetus. Rapid aging of the placenta may reflect underlying medical problem which may restrict normal fetal development.

Structure of the full term human placenta

By term, the mature human placenta is discoid in shape, with an average diameter of 18.5 cm, weight of 500 g, thickness of 23 mm and surface area of 30 000 mm^2. Thickest at its centre and gradually diminishes in thickness towards the periphery. Wide variations in size and shape are found to be within the range of normal and make little difference in function [10].

Being a shared organ between mother and baby, the placenta is formed of a maternal component (decidua basalis) and a fetal component (chorion frondosum). At the fetal side, large chorionic vessels converge toward the umbilical cord. The maternal side of the placenta is dull and is subdivided by grooves and septa into 15-30 lobes. Each lobe contains several cotyledons which consist of a main villus and its branches. The intervillous spaces between fetal and maternal components contain freely circulating maternal blood [1].

Comparative anatomy

Although the placenta possesses the same functions in different mammals, but its structure differs considerably. It can be classified according to Grosser classification which uses the number of the tissues separating maternal blood from fetal blood. Epitheliochorial placenta is the type where chorionic villi grow into the uterine glands (as in sheep, horses, whales and lower primates). In this type, the maternal and fetal blood are separated by epithelium, connective tissue and endothelium. In endotheliochorial placenta, the chorionic villi adhere to the endothelium of maternal blood vessels (as in dogs and cats). However, in hemochorial placenta, the villi penetrate and erode the maternal blood vessels (as in humans, guinea pigs, mice and rats). These differences might affect the placental barrier between mammals, for example, fatty acids cannot traverse the placental barrier in sheep as they do in humans. However, although the human placenta is the same type as placenta of guinea pig, yet IgG is transported across the human placenta but not through that of guinea pig. This wide diversity in placental structure and function among different mammals must be considered when using animal models in medical research [11].

Placental variants

The normal development and structure of the placenta is important for normal fetal development. Multiple placental variants either in shape, insertion of the umbilical cord and variants of implantation are encountered in the medical practice. One of these variants is the *bilobed placenta*, in which the placenta is formed of two nearly equal sized parts separated by a membrane. If the placenta is formed of more than two parts, it is named *multilobate.* In this condition, the umbilical cord may insert in either lobe, or in between the lobes. Although this abnormality may not be associated with fetal anomalies, bilobed placenta may be presented with first-trimester bleeding, polyhydramnios, abruption and retained placenta. Another variant is called *succenturiate placenta* in which one or more accessory lobes develop in the membranes and connect to the

main placental body by vessels of fetal origin. The risk factors which may lead to this condition include advanced maternal age, implantation over leiomyomas or implantation in areas of previous surgery. This abnormality increases the risks of vasa previa and retained placenta [12]

An annularly –shaped placenta is called *circumvallate placenta* which shows depressed center and raised edges composed of a double fold of chorion and amnion. This condition is associated with increased risk of first trimester bleeding, premature rupture of membranes, preterm delivery, and placental abruption [13]. Another rare variant is called *placenta membranacea* where chorionic villi cover fetal membranes either completely or partially. The placenta develops as a thin structure occupying the entire periphery of the chorion. Increased incidence of vaginal bleeding, *placenta previa* and *placenta accreta*, can be associated with this condition [14].

If the umbilical cord is inserted at or near the placental margin rather than in the center, the condition is termed *battledore placenta.* Its incidence is three times more in twin pregnancies than in singltome pregnancies. Complications associated with this condition are preterm labor, fetal distress, and intrauterine growth restriction [13].

Implantation of the placenta in the lower portion of the uterus rather than in the fundus is known as *placenta previa.* In complete previa, the internal cervical os is completely covered by the placenta. In partial previa, the placenta covers a portion of the internal os. In marginal previa, the edge of the placenta extends to the edge of the cervical os. The risk factors include prior cesarean section or other uterine surgery, previous abortion, increasing parity, maternal age and smoking. A woman with a history of *placenta previa* is 12 times more likely to have *placenta previa* in a subsequent pregnancy. Cesarean section is indicated to avoid bleeding from the open vessels that result from dilatation of the cervix and separation of the placenta [15].

Morbidly adherent placenta is a condition called *placenta accreta.* The risk factors increase the incidence of placenta accreta is previous cesarean section, previous uterine surgery, advanced maternal age, high gravidity, previous curettage, and *placenta previa*. Delivery of an adherent placenta can result in hemorrhage, shock, and uterine inversion. If the placental villi penetrate into the myometrium, the condition is termed *Placenta increta.* If the placental villi penetrate through the myometrium to the uterine serosa, it is called *Placenta percreta* [15].

Functions of the placenta

The main function of the placenta is exchange of gases and nutrients. It is responsible for elimination of fetal carbon dioxide and wastes as urea, creatinine and bilirubin as well as transmission of nutrients as glucose, aminoacids, fatty acids and vitamins from maternal to fetal circulation [16].

The placenta also functions as an endocrine organ. It produces the human chorionic gonadotropin, chorionic somatomammotropin and small amounts of chorionic thyrotropin and chorionic corticotrophin. By the end of the 4th month, the placenta forms progesterone to maintain pregnancy and also it produces estriol [6].

Although the placenta allows passage of maternal antibodies to the fetus for protection from some infectious diseases, many bacteria, spirochetes, protozoa and viruses pass through the placenta from mother to fetus and may cause birth defects. Unfortunately, some drugs and their metabolites may traverse the placental barrier and cause serious damage to the developing embryo. Moreover, maternal use of heroin and cocaine may lead to habituation in the baby [6].

Delivery of the placenta

After child birth, placental expulsion occurs within up to half an hour following labor. Passive factors lead to placental separation which can be enhanced by active procedures. Although the placenta provides life to the baby, once maturation of the fetal hypothalamus occurs, the hypothalamic –pituitary axis initiates labor to free the baby and get rid of placenta. Fetal ACTH and oxytocin hormone cause myometrial contractions and distortion of placentome leading to mechanical separation of the placenta. Moreover, delivery of the fetus leads to loss of fetal return to the placenta and subsequently collapse of cotyledonary villi and separation of fetal membranes. Apoptosis of trophoblast cells and endometrial epithelial cells help in placental separation [17]. Separation of the placenta is enhanced by clamping of the umblical cord, controlled cord traction and stimulation of myometrial contraction [18].

Conclusions

Comprehensive understanding of the comparative anatomy between human placenta and other mammals must be considered in medical research. In addition, early detection of placental abnormalities during pregnancy by ultrasonography may help in proper management during pregnancy and labor and to take accurate decisions. Also, thorough examination of the placenta after delivery may orient the attention towards possible retained placental part or to probable fetal problems giving better chance for early intervention.

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