Anatomical Justification for the Use of Human Placenta as a Host for in Vivo Cell and Tissue Transplantation

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ABSTRACT--- ***Authors provide anatomical justification for the use of human placenta as a host for transplanted cells and tissues. A full-term placenta from human donors was prepared for macroscopic visualization. Formalin prepared human cadavers were investigated to identify the optimal site for placenta transplantation. Umbilical vessels of the placenta can provide vascularization of the graft in the body of the recipient and the access of transplant to blood circulation for nutrient delivery and waste removal. The length and the diameter of the placenta arteries and veins provide formation of anastomoses between the placenta and recipient's body. Vascularization of the graft in the body of the recipient can be provided without tension, torsion or inflection of anastomoses. The right iliac site is suggested optional for temporary heterotopic connection of the graft to the body of the recipient, while the hypochondriac and subhepatic regions can be advantageous for the linkage to portal and caval venous systems. Human placenta is suggested appropriate host for auxiliary organ creation.***

Keywords--- human placenta, transplantation, auxiliary organ, vascularization, anastomoses

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1. INTRODUCTION

Problem of poor *in vivo* survival of transplanted cells and tissues is related to the inadequate access of transplant to the blood circulation for nutrient delivery and waste removal. Insufficient blood supply and consequent oxygen and nutrient deficiency as well as exposure to the metabolic toxins causes severe damage and death of cells [1,4,5]. To solve the problem, use of an implantable cell container connected to the circulatory system of the recipient [3,14] as well as transplantation of cells into the vascular tissue [16,19] is recommended. Earlier we reported on the use of small intestinal segments, denude of the mucosal lining and with intact blood supply, as a host for transplantation of the liver tissue fragments and the islets of Langerhans [2,10,12,13]. In order to maintain most of the native vascular structures of the organ and provide anastomoses with the recipient blood circulation, priority is given to the whole-organ decellularization [18]. The placenta is an organ through which oxygen, nutrients as well as wastes are exchanged between the maternal and fetal systems and trans - placental exchange provides all of the metabolic demands of fetal growth and development [6,7,14]. The placenta contains extracellular matrix components and well-preserved endogenous growth factors. Decellularized human placenta is recommended as a dermal substitute for the reconstitution of full-thickness wounds [9] and for adipose tissue engineering [8]. We provide here an anatomical justification for the use of human placenta as a host for creation of auxiliary liver in vivo. At the same time, the benefits of using the placenta in bioengineering with respect to bioethics should be outlined. Once the placenta has completed its function and has been expelled from the body after birth, it is usually abandoned by mothers and is generally regarded as clinical waste. Therefore, use of the placenta in cell and tissue engineering is not related to serious ethical issues concerning the use of human organs in bioengineering [17].

2. MATERIALS AND METHODS

Anatomical study was conducted on 30 full-term placentas from donors [age range of 18 - 38] who gave birth at 37–41 weeks of gestation. Donors signed an informed consent form and the study was approved by the Georgian National Institute of Medical Research Ethical Committee. All the donors had normal pregnancies and delivered healthy newborn babies with weights ranging from 2600 kg to 4100 kg. In order to provide direct 3 dimensional visualization of blood vessels, their ramification and distribution, umbilical cord was trimmed about 10 cm from the insertion and the umbilical vessels were catheterized with 21–24 G intravascular catheters. The blood was flushed out with normal saline containing

5000 units/ml heparin sulfate. Water diluted latex [50%] [NAIRIT L3, Nairi, Armenia] was injected in all placenta samples under the 12 cm H_2O pressure. Inks of different color [red for artery and blue for vein] were added to the mixture for each umbilical vessel. In order to visualize placental vessels 15 placentas were dissected macroscopically after latex injection. The rest 15 placentas were digested in the 80% HCl for 8-10 days at room temperature. Prepared casts were washed in water. The corrosion casting technique has been described in details earlier [10].

To identify the optimal site for transplantation, formalin prepared four human cadavers (2 male and 2 female, mean age 70, the cause of death not related to the illnesses or injury of the abdominal area) were investigated. After opening the abdominal cavity attention was drawn to sub - hepatic space and the left hypochondriac region. Projection area of femoral vessels and the right iliac region was investigated. Criteria for selection of optimal locations of the placenta in the body of the recipient were as following: capacity for graft, proximity of the magistral vessels, providing anastomoses without tension, torsion or inflection as well as possibility of uncomplicated removal of the graft, when necessary.

3. RESULTS AND DISCUSSION

3.1 Vascular architecture of human placenta

The largest vascular trunk of placenta is a first-order blood vessel arising directly from the umbilical cord. Branches of the third order, visible on the fetal surface of the body, sink in the gate area of the cotyledon immediately after the departure from the branches of the first and second order vessels. The branches of the first order as well as the umbilical cord perform mainly transport role, while the branches of the second order carry out mainly the function of distribution. Third order terminal branches plunge under the chorionic plate [Figure 1].

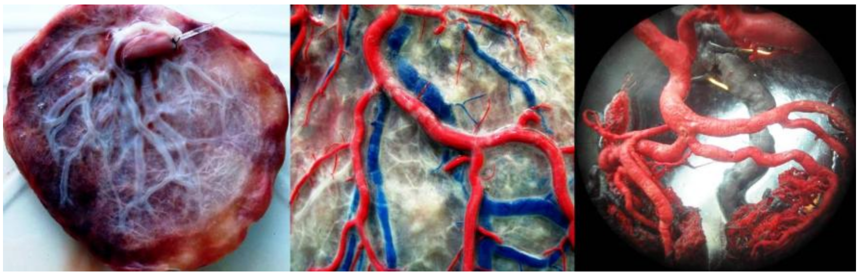

Figure 1. Human placenta: Normal anatomy (on the left side), after the contrast mass injection (in the middle) and corrosion cast (on the right side)

Data obtained confirm the reports on the rich vascularization of human placenta [6,7,14]. Angioarchitectonic of the placenta seems appropriate for the use of the placenta as a host for auxiliary organs. Umbilical vessels of the placenta can provide vascularization of the graft in the body of the recipient and the access of transplant to blood circulation for nutrient delivery and waste removal.

3.2 The placement of placenta in the right hypochondriac region

Blood outflow from the placenta placed under the liver of human recipient [Figure 2] can be provided with the "End-to-side" anastomosis between the inferior vena cava (under the renal veins) of the recipient and placental vein. Blood inflow to the transplant can be provided with the "End-to-side" anastomosis between the portal vein [or portal vein branch] of the recipient and the artery of the placenta. Proximity of large vessels such as portal vein and inferior vena cava provides optimal blood reperfusion of the graft. Residual vessels can be used after the resection of either the right or the left lobe of the liver. The negative aspect of this location is a placement and fixation of large sized placenta graft in subhepatic region as well as repeated manipulations with the portal vein in case of graft removal.

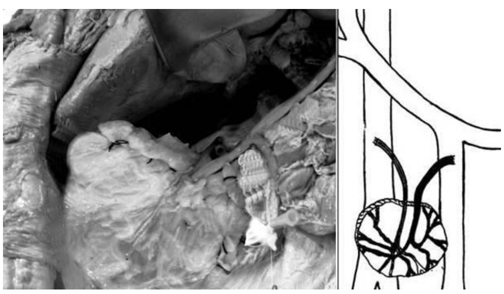

Figure 2. Human placenta placed in right hipochondirac region.

3.3 The placement of placenta in the left hypochondriac region

Blood outflow from the placenta placed in the left hypochondriac region after the removal of the spleen [Figure 3] can be provided with the "End-to-side" anastomosis between the umbilical vein of the placenta and the left renal vein. Blood inflow to the transplant can be provided with the "end-to-end" anastomosis between splenic vein and the umbilical artery of the placenta. The left hypochondriac region can perfectly host human placenta, especially after the removal of the spleen. Anastomoses can be formed similar to the formation of spleno-renal shunts as it is described earlier [11]. However, anatomical variability of the splenic veins may complicate formation of anastomoses between the blood vessels.

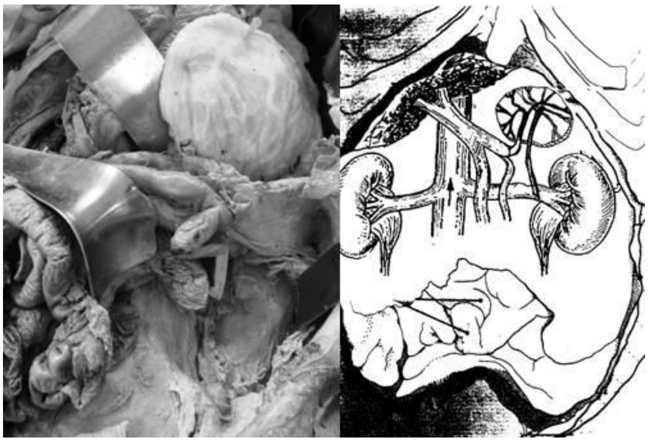

Figure 3. Human placenta placed in left hipochondirac region

3.4 Placement of placenta subcutaneously in the right iliac region

Blood outflow from the placenta placed subcutaneously in the right iliac region [Figure 4] can be provided with the "End- to-side" anastomosis between the umbilical vein of the placenta and the femoral vein of the recipient.

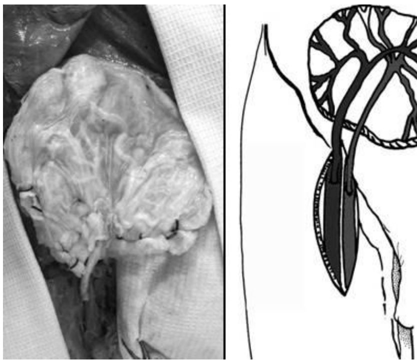

Figure 4. Human placenta placed in right iliac region

Blood inflow to the placenta can be achieved with the „End-to-side" anastomosis between the umbilical artery of the placenta to the femoral artery of the recipient. Extraperitoneal method gives opportunity to avoid the resection of the liver of the recipient and consequent complications. Moreover, grafting method can have temporary, supporting character, such as in the case of the acute liver failure or toxic liver damage. After functional restoration of the liver, graft can be easily removed.

4. CONCLUSIONS

Based on the data obtained, we suggest human placenta appropriate host for auxiliary organ creation. Anatomical structure of the arteries and veins, in particular their length and their diameter allow formation of anastomoses between the placenta and the body of the recipient. Vascularization of the graft in the body of the recipient can be provided without tension, torsion or inflection of the anastomoses. Right iliac site can be optional for temporary heterotopic connection of the graft to the body of the recipient. Hypochondriac and subhepatic regions are suggested advantageous for the linkage to the portal and caval venous system.

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