Effects of Materno-fetal Rhesus Incompatibility on the Histology of Placenta

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Abstract

This study is concerned with the effects of materno-fetal rhesus incompatibility on the histology of full term placenta. For this purpose, two groups of pregnant women were taken, the first group was 10 Rh negative and their husband were Rh positive with previous use of normal vaginal delivery of Rh positive normal babies. Indirect Coomb’s test was done for those women and it was negative indicating previous history Rhesus immunoglobulin containing anti–D antibody within 72 hours after delivery, this means that those women are not sensitised. The second group includes other 10 Rh negative pregnant women, their husbands were Rh positive and they had previous history of intrauterine death or stillbirth, their Indirect Coomb’s test was positive indicating that those women are sensitized and they form immunological reaction against blood cells of their babies. Full term placenta were taken from the two groups and were examined, the results showed significant changes in the structure of the placenta of the second when compared with the first group. In general the placenta of the second group were pallor and heavier than the first group. Histologically, extensive syncytial necrosis, cytotrophoblastic hyperplasia, thickening of the trophoblastic basement membrane with villous edema was found. In the decidua there was decidual necrosis with calcification, fibrinoid deposition and hemorrhage in the intervillous spaces. These results showed that there is an immunologically mediated reaction directed against the placental tissues.

Key words: Placenta, histological changes, Rh incompatibility.

Introduction

Materno-fetal Rhesus incompatibility is defined as a hemolytic disease in newborn babies caused by Rh group incompatibility between mother and child (5). When the fetus inherits red cell antigen determinants from the father which are foreign to the mother, a maternal immune reaction may occur, leading to hemolytic disease in the infant. Basic to such phenomenon are the leakage of fetal red cells into the maternal circulation and in turn transplacental passage of maternal antibodies into the fetus, so immunization of the mother by the blood group antigens on fetal red cells and free passage of antibodies from the mother through the placenta leads to its destruction to reach the fetus (3). Fetal red cells may reach the mother circulation during the last trimester of pregnancy or during child birth itself, thus the mother is now sensitized to the foreign antigens. From the numerous antigens included in the Rh system only the D antigen is the major cause of Rh-incompatibility (15).

The incidence of maternal Rh-isoimmunization has significantly decreased since the use of Rhesus immunoglobulin (Rh Ig) containing anti-D antibodies. Administration within 72 hours of delivery to the Rh negative mothers significantly decrease the risk of hemolytic disease in Rh-positive neonates and in subsequent pregnancies (13). The above introduction indicates that the hemolytic disease has a serious effect on the newborn babies and their placentae during the intrauterine life.

Normal full term placenta composed of two portions: fetal and maternal. The fetal portion called chorionic frondosum which consist of fetal capillaries covered by two layers of trophoblast cells the inner layer is the “cytotrophoblasts” is rarely seen in full term placenta while the outer layer “syncytiotrophoblasts” is commonly seen in full term placenta.

The maternal portion called decidua basalis consist of decidual cells surrounded by collagen fibers (9).
Patients and Methods

Twenty placentae were taken in this study from the pregnant women after labour. Two portions were chosen from each placenta one from the maternal surface the other from the fetal surface of the placenta. These two portions were prepared for light microscopical examination.

Each portion was cut into slices with an average thickness of 3-4 mm. fixed for more then 24 hr. in 10% neutral buffered formalin. The tissues were dehydrated in graded alcohol using two changes of 70%, 90% respectively with a period of one hour each. This is followed by two changes absolute alcohol, the last change of absolute alcohol was left over night, after that the tissue were cleared by two changes of xylene with a period of one hr. each. Finally they were embedded in three changes of 60°C melting point paraffin two hours each. Two blocks from each sample were made, and then a thin section of about 5 µm was cut using Reichert Rotary Microtome (12)

These sections were then mounted on slides to be stained by the following stains:
1- Haematoxylin and Eosin stain.
2- Periodic Acid Schiff’s stain (PAS) stain to demonstrate thickening of trophoblastic basement membrane (1).

Results

The mean weight of the placenta of the second group was more than the first group and the P-value was highly significant (Table 1). The mean weight of the newborn babies in the second group was lower than the first group (Table 1).

In the present study the morphological changes were detected in both the chorionic villi and the maternal decidua basalis indicating that the immunological reaction occurs against all the placental tissues and not against the placental villi only.

In the chorionic villi there were abnormalities in the syncytiotrophoblast indicating delayed villous maturation in addition to shedding and fragmentation of the syncytiotrophoblast. Cytotrophoblastic hyperplasia was observed in the group with Rh incompatibility (Fig.2) as compared with the control group (Fig.1) also their sections showed undu thickening of the trophoblastic basement membrane (Fig.3). There was a decrease in the vascularity of the villi of the placentae of the second group (by counting the number of the capillaries in the villi) in addition to villous edema and stromal fibrosis (Fig.4) within the chorionic villi and intervillous edema in the intervillus space (Fig.5).

Intervillous hemorrhage (Fig.6) was observed in between the chorionic villi while the decidua basalis showed decidual cell necrosis (Fig.7) with calcification (Fig. 8), fibrinoid material deposition was noted indenting the chorionic villi (Fig. 9) and in between the cells of decidua basalis (Fig.10).

Discussion

The histological changes in the placentae of those pregnant women with materno-fetal Rhesus incompatibility is largely due to a reaction within the placental tissues between maternal antibodies and fetal D-antigen (6).

The previous studies on materno-fetal Rhesus incompatibility showed that the histological effects of the immunological reaction against D- antigen found in the chorionic villi while our present study revealed that the reaction occurs against the all placental tissues.

Rhesus hemolytic disease is an immunologically mediated reaction, and there is a strong possibility that the syncytial necrosis is strongly due to immune attack (10).

The placentae obtained from the second group were heavier than those obtained from the first group and this is attributed to many histological changes occurred in their structure.

Burstein and Blumenthal (1992) mentioned that the fluorostein –labeled anti –D localizes mainly on the trophoblastic basement membrane which was the main site for antigen-antibody components deposition, therefore , the thickening of trophoblastic basement membrane might be due to this deposition (7).

The prominent cytotrophoblastic components of the villous trophoblasts which were observed in these placentae obtained from the second group were clearly appeared as a
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result of hyperplasia of these cells in response to syncytial necrosis. The fact that the cytotrophoblastic cells were considered as stem cells for the injured trophoblasts is now well established because in any condition associated with syncytial damage the cytotrophoblastic cells undergo a compensatory hyperplasia in an attempt to replace the injured placentals, a task which appeared to be adequately fulfilled in most placentae from cases of materno-fetal Rhesus incompatibility, this finding is similar to previous studies (6), (10).

Thickening of the trophoblastic basement membrane might be due to the fact that this lamina is secreted by the cytotrophoblastic cells and that their proliferation is accompanied by the secretion of excessive basement membrane material.

The degree and extent of the damage in these placentae was so extensive and could impair the functional efficiency of the placentae leading to reduced blood flow to the fetus and followed by reduction of birth weight of the babies (7).

The syncytial necrosis might be due to narrowing of the intervillous spaces as a result of increased villous size even the cytotrophoblastic hyperplasia is a response to syncytial damage and it is responsible for the changes observed in the basement membrane (10).

Villous edema was recognized as one of the characteristic features in the placentae obtained from those women with Rhesus incompatibility, the cause of the fluid accumulation in the villous stroma may be due to insufficient fetal blood flow (6).

Villous hypovascularity was common in the placentae obtained form women with Rhesus incompatibility. Terminal villi of the mature placenta usually contained between 2-6 capillaries, less than this number with the presence of small and non dilated capillaries were the characteristic features of these placentae.

Hemolytic diseases of the newborn due to Rhesus incompatibility is an immunological disease so the placental changes observed are immunologically mediated (8) because the placentae containing D-antigen that serves as a site for antibody attack and possibly that the immune complexes from the fetal circulation are deposited in the placentae, thus the materno-fetal Rhesus incompatibility is considered as a model for uteroplacental insufficiency and the inadequate placental function contributes to the relatively high fetal death rate due to restricted trophoblastic capacity resulting from an arrest in the villous maturation (7).

The immune complexes might attack the decidual cells and the previous studies showed that the necrosis and death detected in the villi only while in our present study this finding was observed clearly in both placental villi and the deciduas basalis.

Fibrinoid deposition was also common in in these placentae as a result of injury to the syncytiotrophoblast layer followed by mechanical defect in the blood into the intervillous space leading to stasis of the maternal blood and subsequent clotting which in turn stimulates decomposition of fibrinogen into fibrin (14).

Hemorrhage into the intervillous spaces occurred due to vasoconstriction and rupture of the blood vessels as a result of immune attack this finding is similar to was previously found by Biagini et.al, (1992). Lee et.al, (1997) postulated that nitric oxide is normally synthesized by syncytiotrophoblastic cells of the placenta thus destruction and damage of these cells leads to reduced expression of nitric oxide and possibly placental ischemia because nitric oxide is a potent relaxant of the smooth muscle fibers thus vascular constriction and damage will result.

All these placental changes were strongly the result of an immune reaction within the placental tissues between the maternal antibodies and the fetal D-antigen.
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References


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Figure (1): Light microscopical (LM) appearance of normal term placenta showing the chorionic villi (CV) and the decidua basalis (D) (H&E X100).

Figure (2): (LM) appearance of the placenta from the second group showing cytotrophoblastic hyperplasia (arrows) with fibrin deposition (F) within the chorionic villi (PAS X10).

Figure (3): Light microscopical appearance of the placenta from the second group showing thickening of the trophoblastic basement membrane (arrows) (PAS X100).

Figure (4): Light microscopical appearance of the placenta from the second group showing hypovascular villi with villous edema and stromal fibrosis (arrows) of the chorionic villi (H&E X100).
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Figure (5): Light microscopical appearance of the placenta from the second group showing intervillous edema (IVE) in between the chorionic villi (CV) (H&E X100).

Figure (7): Light microscopical appearance of the placenta from the second group showing decidual cell necrosis (arrows) (H&E X100).

Figure (6): Light microscopical appearance of the placenta from the second group showing intervillous haemorrhage (IVH) in between the chorionic villi (H&E X100).

Figure (8): Light microscopical appearance of the placenta from the second group showing decidual cell calcification (arrows) (H&E X100).
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Figure (9): Light microscopical appearance of the placenta from the second group showing fibrinoid material (F) deposition within the villous stroma (PAS X100).

Figure (10): Light microscopical appearance of the placenta from the second group showing fibrinoid material (F) deposition in between the cells of decidua basalis (PAS X100).