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Changes in Placental Hofbauer Cell Numbers in Histological Chorioamnionitis

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ABSTRACT

Background: *Hofbauer cell (HBC), named by Isfred Hofbauer, is a cell that occurs in the placental villi from 18 days of gestation to the end of pregnancy, located near fetal blood vessels and trophoblasts, and is considered to play important role in placental formation and homeostasis. Hofbauer cells are a member of the mononuclear macrophage family, generally round long cells, 10-30㎛ in size, and exhibit pleomorphic nature with high degree of vacuolization by the plasma granules. Currently, we believe that these cells originate from stem cells of interstitial villus in early pregnancy and differentiate from fetal monocytes in the second half of pregnancy. In obstetric practice, Hofbauer cells are considered to play important role in the establishment of normal pregnancy and pathogenesis of abnormal pregnancy.* ***The aim:*** *We aimed to investigate the changes in placental Hofbauer cell numbers in histological chorioamnionitis.* ***Methods:*** *The study population included 279 placentas delivered for the past two years.* ***The Results:*** *Tissue sections were obtained from the placenta, followed by conventional tissue sampling, H-E stained specimens were prepared under ×100 light microscope view, and inflammatory changes were observed, normal (control group) if no change was observed, HCAM (study group) if change was present, HCAM was again diagnosed as HCAM if inflammatory changes were present in the extrachorionic wall, and in both chorionic and amniotic membranes if they were involved in the extrachorionic wall, according to Blanc's classification. Changes in placental Hofbauer cell numbers were performed by calculating the average number of cells in any five transverse sites under ×400 light microscope view of placental tissue samples for obstetric and clinical parameters such as amniotic fluid count, amniotic fluid phase, senescence, fetal and neonatal asphyxia (Apgar score below 7) according to the stage of HCAM.* ***Conclusions:*** *The changes in Hofbauer cell numbers in histological chorioamnionitis are as follows. Hofbauer cell numbers were significantly higher, with average of 3.1 in histological chorioamnionitis stage 1, 5.0 in stage 2, and 6.7 in stage 3, compared with the normal placenta(2.0). Hofbauer cell counts were significantly higher in all stages of amniotic fluid turbidity, senescence >2 degrees, and fetal and neonatal asphyxia in terms of obstetric and clinical parameters.*

Keywords: Placental, Hofbauer cell, and Histological chorioamnionitis.

Article Information

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INTRODUCTION

Hofbauer cell (HBC), named by Isfred Hofbauer, is a cell that occurs in the placental villi from 18 days of gestation to the end of pregnancy located near fetal blood vessels and trophoblasts and is considered to play important role in placental formation and homeostasis. Hofbauer cells are a member of the mononuclear macrophage family, generally round long cells, 10-30㎛ in size and exhibit pleomorphic nature with high degree of

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vacuolization by the plasma granules[2,4,5]. Currently, we believe that these cells originate from stem cells of interstitial villus in early pregnancy and differentiate from fetal monocytes in the second half of pregnancy.

In obstetric practice, Hofbauer cells are considered to play important role in the establishment of normal pregnancy and pathogenesis of abnormal pregnancy[1,3,7]. These cells are important not only for protecting the fetus and for developing resistance but also for the causal analysis of abnormal pregnancy outcomes.

According to the literature, Hofbauer cells play direct role in the early development of the placenta with significant decrease in placenta in the placenta starting from the fourth month of gestation with significant differences in the number of Hofbauer cells in the early placenta and placenta. While the role of Hofbauer cells in physiological and pathological processes extends to tissue damage, inflammation and tumor development, it is known that these cells play key role in stimulating new tissue growth[3,6].

On the other hand, since Hofbauer cells have been shown to be capable of synthesizing prostaglandin E2 and thromboxane in vitro, they are thought to have role in the regulation of blood pressure in placental vessels. In obstetric practice, chorioamnionitis is important condition of intrauterine infection leading cause of early abortion and early delivery. We recommend that Hofbauer cells promote the maturation and development of the placental stroma and therefore focus on the dynamics of these cell changes in various abnormal pregnancies such as abortion and preterm delivery.

Studies on changes in Hofbauer cell numbers and changes in gene expression in several pregnancy complications such as other gestational diabetes, preeclampsia, and cytomegalovirus infection, the main cause of congenital infections are being attempted.

We aimed to investigate the changes in placental Hofbauer cell numbers in histological chorioamnionitis.

SUBJECTS AND METHODS

The study population included 279 placentas delivered at the Pyongyang Maternity Hospital for the past two years.

Multiple pregnancies or malformation were excluded from the study.

First, tissue sections were obtained from the placenta, followed by conventional tissue sampling, H-E stained specimens were prepared under ×100 light microscope view and inflammatory changes were observed, normal (control group) if no change was observed, HCAM (study group) if change was present, HCAM was again diagnosed as HCAM if inflammatory changes were present in the extrachorionic wall, and in both chorionic and amniotic membranes if they were involved in the extrachorionic wall according to Blanc's classification. The prevalence of HCAM was 72 (25.8%) of 279 patients, of whom 35 (12.5%), 23 (8.2%) and 14 (5.0%) had stage 3 disease.

Changes in placental Hofbauer cell numbers were performed by calculating the average number of cells in any five transverse sites under ×400 light microscope view of placental tissue samples for obstetric and clinical parameters such as amniotic fluid count, amniotic fluid phase, senescence, fetal and neonatal asphyxia (Apgar score below 7) according to the stage of HCAM. Significance tests were performed by Student's t-test for the mean of the study results and by Chi-square test for the percentage of the study results. The clinical pathological diagnosis and diagnosis of histological chorioamnionitis were made according to clinicopathological diagnosis and treatment guidelines published by the Ministry of Public Health, DPRK.

RESULTS

Table 1. Changes of the number of HBC according to the stages in HCAM.

classificaion		cases	$\overline{X}$ ±SE(n)	P		
				P1	P2	P3
Normal placenta		30	2.0±0.1	-		
HCAM	Stage 1	35	3.1±0.2	<0.05	-	
	Stage 2	23	5.0±0.3	<0.05	<0.05	-
	Stage 3	14	6.7±0.4	<0.05	<0.05	<0.05

As shown in Table 1, the number of Hofbauer cells per stage in histological chorioamnionitis was significantly higher than that in normal placenta, with significant increase in stage III.

Table 2. Variation of the number of HBCs per amniotic fluid in HCAM ($\overline{X}$ ±SE, n).

Classification		Cases	Amniotic fluid amount		
			~29㎜	30~50㎜	51㎜~
Normal placenta		30	1.9±0.1	2.1±0.1	2.0±0.2
HCAM	Stage 1	35	3.7±0.2*△	3.0±0.2*	3.1±0.3*
	Stage 2	23	4.5±0.3*	5.1±0.3*	5.6±0.6*△
	Stage 3	14	7.4±0.7*	6.4±0.5*	-

**; p<0.05 (compared with normal placenta) △; p<0.05 (comparison with amniotic fluid).*

As shown in Table 2, the number of Hofbauer cells per amniotic fluid in histological chorioamnionitis was significantly higher in all stages of amniotic fluid compared with normal placenta while in amniotic fluid, the number was significantly higher in stages 1 and 51 mm to 3 at ~29 mm.

Table 3. Number change of HBC per amniotic fluid phase in HCAM ($\overline{X}$ ±SE, n).

Classification		Cases	Amniotic fluid phase	
			clear	turbidity
Normal placenta		30	1.8±0.1	2.6±0.1
HCAM	Stage 1	35	2.9±0.2*	4.4±0.1*△
	Stage 2	23	4.6±0.3*	6.1±0.2*△
	Stage 3	14	5.0±0.6*	7.6±0.3*△

**; p<0.05 (compared with normal placenta) △; p<0.05 (compared with amniotic fluid phase)*

As shown in Table 3, the number of Hofbauer cells per amniotic fluid phase in histological chorioamnionitis was significantly higher in all stages of amniotic fluid phase compared with normal placenta and in amniotic fluid phase, the number was significantly higher in all stages in opacity.

Table 4. Variation in the number of HBCs per Aging Grade in HCAM ($\overline{X}$ ±SE, n.)

Classification		Cases	Senescence grade		
			1	2	3
Normal placenta		30	1.6±0.1	2.1±0.1	2.1±0.7
HCAM	Stage 1	35	2.7±0.5*	4.6±0.6*△	-
	Stage 2	23	3.1±0.2*	4.9±0.3*△	6.5±0.5*△
	Stage 3	14	4.5±0.3*	6.1±0.4*△	7.4±0.8*△

**; p<0.05 (compared with normal placenta) △; p<0.05 (compared with Senescence grade).*

As shown in Table 4, the number of Hofbauer cells per senescence grade in histological chorioamnionitis was significantly higher in all stages of senescence except stage 1 at age 3 compared to normal placenta and in senescence grade 3 was significantly higher in all stages of grade 2 and 3 except stage 1 at stage 3.

Table 5. Changes in the number of HBC by fetal and neonatal screening in HCAM ($\overline{X}$ ±SE, n.)

Classification		Cases	Fetal and neonatal asphyxia	
			-	+
Normal placenta		30	1.8±0.1	2.6±0.1△
HCAM	Stage 1	2.9±0.2*	4.5±0.1*△	4.4±0.1*△
	Stage 2	3.8±0.4*	5.9±0.1*△	6.1±0.2*△
	Stage 3	5.0±0.6*	7.6±0.3*△	7.6±0.3*△

**; p<0.05 (compared with normal placenta) △; p<0.05 (compared with asphyxia)*

As shown in Table 5, the number of Hofbauer cells per fetal and neonatal screening for histological chorioamnionitis was significantly higher in all stages of asphyxia compared with the normal placenta and in asphyxia, the number was significantly higher in all stages when asphyxia was present.

DISCUSSION

Chorioamnionitis(CAM) is histopathological diagnosis of inflammation in the chorionic and amniotic membranes. In 1959, the CAM was divided into stages 1 and 3 according to histopathological findings of the follicular membrane grafted to the internal uterine bulb (Blanc classification) : leukocyte infiltration to the extrachorionic wall, no infiltration to the perichorionic wall, stage 1 infiltration to the chorionic wall, stage 2 infiltration to the chorionic membrane, stage 3 infiltration to the chorionic membrane, stage 1, stage 2 CAM and stage 3 CAM. CAM is also divided into clinical chorioamnionitis (Clinical CAM; CCAM) and histopathological chorioamnionitis (Histological CAM; HCAM) which means sheep-sensitive inflammation or placentitis for CAM stage 3.

The causative bacteria of CAM are mainly staphylococci, streptococci, Escherichia coli, Pseudomonas aeruginosa, gonorrhoeae, and anaerobic. CAM is 95% in abortions below 25 weeks of gestation, 35-40% in preterm labour between 25-32 weeks, 11% in preterm labour between 33-35 weeks, and 5% in term, and CAM is the major cause of preterm labour in preterm labour cases without electropulmonary rupture. CAM is the main cause of postpartum sepsis, postcesarean infection, postepisiotomy infection, and postpartum endometritis. On the other hand, the changing number of Hofbauer cells in obstetric practice with regard to changes in Hofbauer cell numbers in diseases such as chorioamnionitis, preeclampsia, viral infection, and diabetes, highlights the role of changes in Hofbauer cell numbers in the development of abnormal pregnancy or pregnancy-related complications.

Our histological chorioamnionitis showed significant increase in stage 3 Hofbauer cell numbers with 3.1±0.2 at stage 1, 5.0±0.3 at stage 2, and 6.7±0.4 at stage 3 compared with 2.0±0.1 at stage 3 ($p<0.05$, Table 1). This suggests that the number of Hofbauer cells in the placenta of HCAM is approximately three times normal in the third stage and that

Hofbauer cells may be microscopic diagnostic marker of HCAM. We found that the number of Hofbauer cells per amniotic fluid in histological chorioamnionitis was significantly greater in the normal placenta.

The positive water content was significantly higher in the first and third stages at ~29 mm ($p<0.05$ Table 2). This suggests that the incidence of HCAM is also related to amniotic fluid, and that in oligohydramnios, inflammatory changes are present in the amniotic membrane and in the amniotic membrane in oligohydramnios, while in many cases inflammatory changes are present in the extrachorionic wall.

We found that the number of Hofbauer cells per amniotic fluid phase in histological chorioamnionitis was significantly greater for clear placenta(Table 3). This is in good agreement with the results of one study or the previous study (Table 8) showing higher incidence of HCAM in amniotic turbidity, as result of study showing greater prevalence of HCAM in amniotic turbidity. We found that Hofbauer cell counts for each grade of senescence in histological chorioamnionitis were significantly different for normal placenta.

Aging was significantly higher in all stages of grade 2 and 3 except stage 1 at grade 3 ($p < 0.05$ Table 4). The results of the above study also show that higher placental age is associated with higher HCAM incidence and higher Hofbauer cell numbers.

We found that the number of Hofbauer cells per fetus and neonate for histological chorioamnionitis was significantly greater for normal placenta without asphyxia. In the household screening, the number of households was significantly higher in all stages when households were present ($p<0.05$ Table 5). This suggests that, if placenta with normal pregnancy or HCAM is involved in asphyxia, Hofbauer cells are enriched compared to normal delivery and if histopathological examination of placenta delivered after delivery in obstetric practice shows an increase in Hofbauer cells it can be used as a marker to predict neonatal asphyxia and to establish a viable strategy.

Thus, we have established a variety of placental Hofbauer cell counts in histological chorioamnionitis with the basis for the management of placental Hofbauer cell counts in obstetric practice in abnormal pregnancies or in multiple pregnancies leading to preterm birth, fetal and neonatal distress, or in various pregnancy-related complications.

CONCLUSION

The changes in Hofbauer cell numbers in histological chorioamnionitis are as follows.

1) Hofbauer cell numbers were significantly higher with average of 3.1 in histological chorioamnionitis stage 1, 5.0 in stage 2, and 6.7 in stage 3 compared with the normal placenta(2.0).

2) Hofbauer cell counts were significantly higher in all stages of amniotic fluid turbidity, senescence >2 degrees, and fetal and neonatal asphyxia in terms of obstetric and clinical parameters.

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