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Placental Pathology in Intrauterine Growth Retardation

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Background : Histologic examination of the placentas from intrauterine growth retardation (IUGR) fetuses can supplement clinical knowledge of the cause of IUGR. The present study was undertaken to observe the pathologic findings regarding the placentas in IUGR fetuses. **Methods :** Clinicopathologic findings in 45 cases with IUGR at the third-trimester were reviewed, and they were compared with those of 24 normal control cases. An IUGR fetus was defined as one with a birth weight less than those in the 10th percentile. Of the IUGR cases, 15 were hypertensive IUGR with or without preeclampsia, and 30 were normotensive IUGR. **Results :** The IUGR groups had significantly shorter mean gestational ages, lower mean placental weights, and higher incidences of oligohydramnios, compared to the normal controls ($p<0.05$). Histologically, IUGR was characterized by increased incidence of decidual vasculopathy (31.1%, $p<0.05$), multiple and severe infarct ($p<0.05$), villous fibrosis (31.1%, $p<0.05$), syncytiotrophoblastic knots (86.7%, $p<0.05$), and higher degree of increased perivillous fibrin deposition ($p<0.05$). However, there were no statistically significant differences in the placental lesions between hypertensive and normotensive IUGR cases, except for the presence of decidual vasculopathy. **Conclusions :** Abnormal uteroplacental vasculature and chronic uteroplacental insufficiency, coagulation-related pathology in the uteroplacental, intervillous and/or fetoplacental vasculature, and chronic inflammatory lesions may be the primary disease processes related to the placental pathology of IUGR. Although the cause of IUGR pregnancies is heterogeneous, careful cilinicopathologic correlations in individual cases are necessary in the interpretation of placental lesions of IUGR, and the total burden of several placental lesions may be more important than a single histologic feature.

Key Words : Fetal Growth Retardation-Placenta-Pathology

The infant born with intrauterine growth retardation (IUGR) is recognized as having an increased risk of in utero mortality, neonatal morbidity and mortality, and long-term neurological complications.[1,2] Known causes of IUGR can be traced in up to 40% of cases studied, including maternal diseases and fetal or placental factors,[3,4] and the remainder of IUGR cases are idiopathic in origin. Among the large numbers of maternal factors, maternal hypertension (especially preeclampsia or eclampsia) is one of the most important factors in IUGR. Pregnancy induced hypertension associated placental pathology include infarct, retroplacental hemorrhage, accelerated maturation, fibromuscular hyperplasia and obliterative endarteritis of the fetal stem artery, villous edema, stromal fibrosis, increased number of syncytial knots, cytotrophoblast hyperplasia, trophoblast basement membrane thickening, deficiency of the vasculosyncytial membrane, excessive fibrinoid necrosis, and acute atherosis in decidual vessels.[1,2] Maternal factors include cardiac disease, pulmonary or renal disease, anemia, and connective tissue disease. Fetal factors include chromosomal abnormalities, ventral wall defect, or genitourinary defects. The known placental pathology of an IUGR infant includes decrease of placental growth, maternal vasculopathy, chronic villitis, increase of perivillous fibrin, fetal thrombotic arteriopathy and avascular villi as its secondary feature, umbilical cord anomaly, infarct, cytotrophoblast hyperplasia, basement membrane thickening, etc.[2,3] Histologic examination of the placentas from IUGR fetuses can supplement clinical knowledge of the cause of IUGR. The present study was undertaken to investigate the pathologic findings regarding the placentas in IUGR fetuses.

MATERIALS AND METHODS

Placental tissue samples were obtained from 45 singleton

third-trimester pregnancies complicated by IUGR and from 24 normal uncomplicated term pregnancies appropriate for gestational age (AGA). An IUGR fetus was defined as one with a birth weight less than those in the 10th percentile. Birth weight percentiles were determined by previously published normal curves.[5] Maternal data were obtained from the medical records of the IUGR and AGA cases studied. For all patients included in the data set, the gestational age was estimated from the last menstrual period or early ultrasonogram before the 12th week's gestation. The cases for which neonatal and obstetric assessments differed by 2 weeks were excluded. The final data set was composed of 45 third-trimester pregnancies complicated by IUGR for which birth weights and APGAR scores were available. Because preeclampsia is an important maternal factor associated with IUGR, the IUGR cases were further divided into two subgroups according to the presence of maternal hypertension. The hypertensive IUGR group consisted of 15 cases: 11 with preeclampsia, two with eclampsia, one with chronic hypertension aggravated by preeclampsia, and one with chronic hypertension. The normotensive IUGR group consisted of 30 cases, including one case with maternal gestational diabetes. All of the IUGR samples were collected from the delivery suite of the Samsung Cheil Hospital between Jan. 1997 and Dec. 1998. The normal control group was selected at random from the same hospital between Jan. and Feb. 1999; the birth weights of all of these infants were ≧10th percentile. Samples were taken from both vaginal deliveries (assisted and normal) and cesarean sections. Cases consisting of twins were not included.

Placental examinations were performed according to a modification of Benirschke's method,[6] and all placentas were examined by pathologists. The placentas were weighed following removal of adherent blood, umbilical cords and extraplacental membranes. Placental weight percentiles were determined according to the published normal curve.[7] For each case, one to two samples of umbilical cords, one to two samples of extraplacental membranes, and two to four samples of parenchyma were available for review. Gross pathologic diagnoses were confirmed microscopically. Placental histologic data included decidual vasculopathy, retroplacental hematoma, fetal thrombotic arteriopathy, chorangiosis, acute inflammation (acute necrotizing deciduitis, acute chorioamnionitis or subchorionitis, acute funisitis and umbilical vasculitis), chronic deciduitis, intervillous thrombus and microcalcification. The presence, or absence, of these lesions was used in the analysis. Decidual vasculopathy was defined as fibrinoid necrosis with or without atherosis, and/or accompanied by vasculitis.[2] Chorangiosis was diagnosed using the criteria by Altshuler.[8] A few decidual lymphocytic infiltrations are normally present in the decidua of the basal plate, and these cases are excluded in the diagnosis of chronic deciduitis. Only dense lymphoid infiltration or destructive, necrotizing inflammation is considered to have deciduitis.[2] Also, the presence and severity of infarct were evaluated and graded as focal (one focus), multifocal (at least two separate foci) and massive (occupying more than 50% of the placental volume). The severity of increased syncytiotrophoblastic (ST) knotting were graded as mild and severe. The pattern of the ST knotting was recorded as localized if the feature of increased ST knotting was focally or multifocally observed around the localized areas associated with infarct or fetal vessel occlusion, and as diffuse when the finding was not associated with any other histologic findings. The presence of villous hypovascularity, villous fibrosis, villous edema, and chronic villitis was assessed as absent, focal, multifocal, and diffuse. However, only the presence, or absence of these lesions was used in the final analysis since positive cases are small in number. The presence and degree of perivillous fibrin deposition were recorded as no or mildly increased, moderately increased, or severely increased. Two pathologists reviewed the slides together and scored these lesions with agreement. The pathologists were blinded to clinical data except the gestational ages.

Analyses of variance and chi-square analysis were used to determine significance (defined as $p<0.05$).

RESULTS

Table 1 presents the fetal and maternal characteristics of the present data set. The ages of the mothers were not significantly different in the three groups. The gestational ages, birth weights, and placental weights were significantly different in these groups; the hypertensive IUGR cases were delivered at significantly younger gestational ages than were the AGA and normotensive

Table 1. Mean values for maternal and fetoplacental characteristics of AGA, normotensive IUGR, and hypertensive IUGR infants

	AGA (n=24)	Normotensive IUGR (n=30)	Hypertensive IUGR (n=15)
Age of mother (yr)	28.7±2.7	30.5±4.4	29.3±3.1
Gestational age (wk)[a]	39.7±1.0	37.7±2.3	35.6±2.1
Birth weight (g)[a]	3,285±334	2,171±388	1,860±430
Placental weight (g)[a]	475±69	317±77	306±54

AGA: appropriate for gestational age, IUGR: intrauterine growth retardation, yr: year, wk: week.
[a]: $p<0.05$.

Table 2. Comparisons of clinical features of AGA and IUGR groups

Clinical finding	AGA (n=24)	Combined IUGR (n=45)	Normotensive IUGR (n=30)	Hypertensive IUGR (n=15)
APGAR score <7 (1 min)	0%	6 (13.3%)	2 (6.7%)	3 (20%)
APGAR score <7 (5 min)	0%	3 (6.7%)	1 (3.3%)	2 (13.3%)
Oligohydramnios[a]	2 (8.3%)	22 (48.9%)	18 (60%)	4 (26.7%)
Hx. of IUGR	0%	1 (2.2%)	1 (3.3%)	0%
Hx. of IUFD	0%	4 (8.9%)	2 (6.7%) (2 times in one case)	2 (13.3%)
Hx. of habitual abortion (≧3)	0%	1 (2.2%)	0%	1 (6.7%)
Hx. of twin pregnancy	0%	2 (4.4%)	1 (3.3%)	1 (6.7%)
Uterine myoma	1 (4.2%)	2 (4.4%)	0%	2 (13.3%)
Hx. of uterine synechiae	0%	2 (4.4%)	2 (6.7%)	0%
Associated fetal vessel anomaly	0%	2 (4.4%)	2 (6.7%)	0%
Mode of delivery				
Cesarean section	0%	29 (64.4%)	18 (60%)	11 (73.3%)
Normal and assisted delivery	24 (100%)	16 (35.6%)	12 (40%)	4 (26.7%)
PROM	5 (20.8%)	5 (11.1%)	4 (13.3%)	1 (6.7%)

AGA: appropriate for gestational age, IUGR: intrauterine growth retardation, Hx.: history, PROM: premature rupture of membrane.
[a]: $p<0.05$ comparison between AGA and combined IUGR.

Table 3. Gross abnormalities of placenta in AGA and IUGR groups

AGA (n=24)	Normotensive IUGR (n=30)	Hypertensive IUGR (n=15)
Marginal insertion of cord (1)	Cord around neck (clinical finding) (2)	Accessory lobe (1)
Chorangioma, small (1)	Placenta accreta (clinical finding) (2)	Cord around neck & trunk (1)
Circummargination (1)	True knot of umbilical cord (1)	
Circumvallation (1)	Atrophy of one umbilical artery (1)	
	Membranous insertion of cord (1)	
	Circummargination (1)	
	Circumvallation (1)	
	Accessory lobe (1)	
	Placenta previa marginalis (1)	
	Amnion nodosum (1)	

AGA: appropriate for gestational age, IUGR: intrauterine growth retardation.

IUGR cases, and the normotensive IUGR cases were delivered at significantly younger gestational ages than were the AGA cases ($p<0.05$). The birth weights and the placental weights were significantly lower in the hypertensive IUGR cases, compared to those of the AGA and normotensive IUGR cases. and those of the normotensive IUGR cases were significantly lower than those of the AGA cases ($p<0.05$). The IUGR group had placental weight less than the 10th percentile for gestational age in 71.1% (32 out of 45 cases). In contrast, no AGA case had placental weights less than the 10th percentile for gestational age. The proportions of male and female infants in the IUGR and control cases were not significantly different.

The comparisons of maternal history of previous IUGR, intrauterine fetal death, habitual abortions, twin pregnancy, mode of delivery, and other clinical features are presented in Table 2. The IUGR groups were associated with a higher incidence of oligohydramnios ($p<0.05$) and a low APGAR score.

The gross abnormalities of the placentas are presented in Table 3. The gross abnormalities of the placentas found in the IUGR cases were accessory lobe (two cases), true knot of cord (one case), atrophy of one umbilical artery (one case), membranous insertion (one case), circumvallation (one case), circummargination (one case), and amnion nodosum (one case). Clinical data revealed that two of the IUGR cases involved the cord around the neck or trunk, two cases involved placenta accreta, and one case involved placenta previa marginalis. The AGA group consisted of one case each of marginal insertion, small chorangioma, circummargination and circumvallation. The histologic findings are presented in Table 4 and 5. Decidual vasculopathy (Fig. 1A) was observed in 31.1% (14 out of 45) of the IUGR cases as a whole group, but no AGA case had decidual vasculopathy. The incidence of villous infarct (Fig. 1B) including focal lesion was significantly higher in the IUGR cases (40%, 18 out of 45) than in the AGA cases (4.2%, 1 out of 24) (Data

Table 4. Placental histologic features in AGA and IUGR groups

AGA (n=24)	Normotensive IUGR (n=30)	Hypertensive IUGR (n=15)
Fetal thrombotic vasculopathy (1)	Decidual vasculopathy (7)	Decidual vasculopathy (7)
Retroplacental hematoma (1)	Multifocal or massive infarct (9)	Multifocal or massive infarct (3)
Mild inc. of ST knots (12)	Fetal thrombotic vasculopathy (3)	Fetal thrombotic vasculopathy (1)
Severe inc. of ST knots (3)	Chorangiosis (4)	Chorangiosis (3)
Localized inc. of ST knots (11)	Mild inc. of ST knots (15)	Retroplacental hematoma (2)
Diffuse inc. of ST knots (4)	Severe inc. of ST knots (11)	Mild inc. of ST knots (5)
Villous hypovascularity (2)	Localized inc. of ST knots (15)	Severe inc. of ST knots (8)
Villous fibrosis (2)	Diffuse inc. of ST knots (11)	Localized inc. of ST knots (9)
Villous edema (4)	Avascular terminal villi (1)	Diffuse inc. of ST knots (4)
Mod. to severe inc. of PVF (1)	Villlous hypovascularity (8)	Villous hypovascularity (1)
Intervillous thrombus (1)	Villous fibrosis (11)	Villous fibrosis (3)
Chronic villitis (2)	Villous edema (3)	Villous edema (2)
Acute necrotizing deciduitis (3)	Mod. to severe inc. of PVF (7)	Mod. to severe inc. of PVF (5)
Acute chorioamnionitis (7)	Intervillous thrombus (6)	Intervillous thrombus (4)
Calcification (18)	Chronic villitis (2)	Chronic villitis (2)
	Acute necrotizing deciduitis (5)	Acute necrotizing deciduitis (4)
	Acute chorioamnionitis (1)	Acute chorioamnionitis (3)
	Acute funisitis (1)	Acute funisitis (1)
	Chronic deciduitis (2)	Calcification (7)
	Calcification (22)	

Inc: increase, ST: syncytiotrophoblastic, Mod: moderate, PVF: perivillous fibrin.

Table 5. Comparison of placental features to the pattern of IUGR

Histologic findings	AGA (n=24)	Combined IUGR (n=45)	p-value	Normotensive IUGR (n=30)	Hypertensive IUGR (n=15)	p-value
Decidual vasculopathy	0 (0%)	14 (31.1%)	<0.05	7 (23.3%)	7 (46.7%)	NS
Villous infarct						
Absent or focal	24 (100.0%)	33 (73.3%)	<0.05	21 (70.0%)	12 (80.0%)	NS
Multifocal or massive	0 (0%)	12 (26.7%)		9 (30.0%)	3 (20.0%)	
Fetal thrombotic vasculopathy	1 (4.2%)	4 (8.9%)	NS	3 (10.0%)	1 (6.7%)	NS
Retroplacental hematoma	1 (4.2%)	2 (4.4%)	NS	0 (0%)	2 (13.3%)	NS
Chorangiosis	0 (0%)	7 (15.6%)	NS	4 (13.3%)	3 (20.0%)	NS
Increased ST knots	15 (62.5%)	39 (86.7%)		26 (86.7%)	13 (86.7%)	
Degree: mild	12 (50%)	20 (44.4%)	<0.05	15 (50%)	5 (33.3%)	NS
severe	3 (12.5%)	19 (42.2%)		11 (36.7%)	8 (53.3%)	
Pattern: localized	11 (45.8%)	24 (53.3%)	NS	15 (50.0%)	9 (60.0%)	NS
diffuse	4 (16.7%)	15 (38.3%)		11 (36.7%)	4 (26.7%)	
Avascular terminal villi	0 (0%)	1 (2.2%)	NS	1 (3.3%)	0 (0%)	NS
Villous hypovascularity	2 (8.3%)	9 (20.0%)	NS	8 (26.7%)	1 (6.7%)	NS
Villous fibrosis	2 (8.3%)	14 (31.1%)	<0.05	11 (36.7%)	3 (20.0%)	NS
Villous edema	4 (16.7%)	5 (11.1%)	NS	3 (10.0%)	2 (13.3%)	NS
Perivillous fibrin						
No or mild increase	23 (95.8%)	33 (73.3%)	<0.05	23 (76.7%)	10 (66.7%)	NS
Moderate or severe increase	1 (4.2%)	12 (26.7%)		7 (23.3%)	5 (33.3%)	
Intervillous thrombus	1 (4.2%)	10 (22.2%)	NS	6 (20.0%)	4 (26.7%)	NS
Chronic villitis	2 (8.3%)	4 (8.9%)	NS	2 (6.7%)	2 (13.3%)	NS
Acute nec. deciduitis	3 (12.5%)	9 (20.0%)	NS	5 (16.7%)	4 (26.7%)	NS
Acute chorioamnionitis	7 (29.2%)	4 (8.9%)	<0.05	1 (3.3%)	3 (20.0%)	NS
Acute funisitis	0 (0%)	2 (4.4%)	NS	1 (3.3%)	1 (6.7%)	NS
Chronic deciduitis	0 (0%)	2 (4.4%)	NS	2 (6.7%)	0 (0%)	NS
Calcification	18 (75.0%)	29 (64.4%)	NS	22 (73.3%)	7 (46.7%)	NS

ST: syncytiotrophoblastic, Mod: moderate, Nec.: necrotizing, IUGR: Intrauterine growth retardation, AGA: appropriate for gestational age.

not shown in Table 5). Also, IUGR cases tended to have multifocal infarcts (26.7%, 12 out of 45); whereas, there was no AGA case with multifocal or massive infarct. The incidence of increase of ST knots (Fig. 2) was significantly higher in the IUGR cases

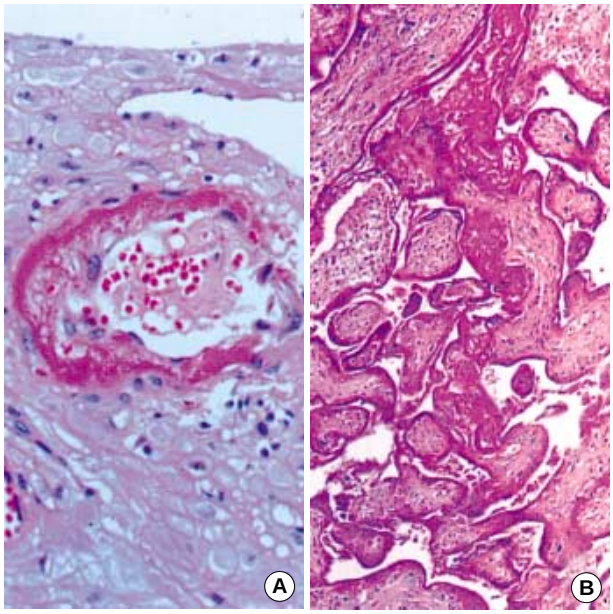

Fig. 1. An IUGR case associated with eclampsia showing decidual vasculopathy (A) and villous infarct (B). A: A decidual vessel shows fibrinoid necrosis of vessel walls and a perivascular mononuclear infiltrate. B: Infarcted area shows aggregation of ghost-like necrotic villi.

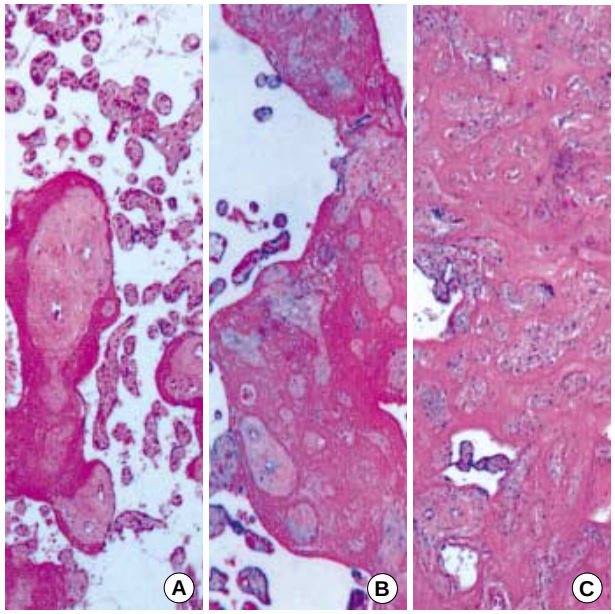

Fig. 3. Increase of perivillous fibrin were assessed as normal or mildly increased (A), moderately increased (B), and severely increased (C).

(86.7%, 39 out of 45) than in the AGA cases (62.5%, 15 out of 24), and those cases with severe increases were frequently observed in the IUGR group (42.2%, 19 out of 45 cases) compared to the AGA group (12.5%, 3 out of 24 cases). Villous fibrosis was in

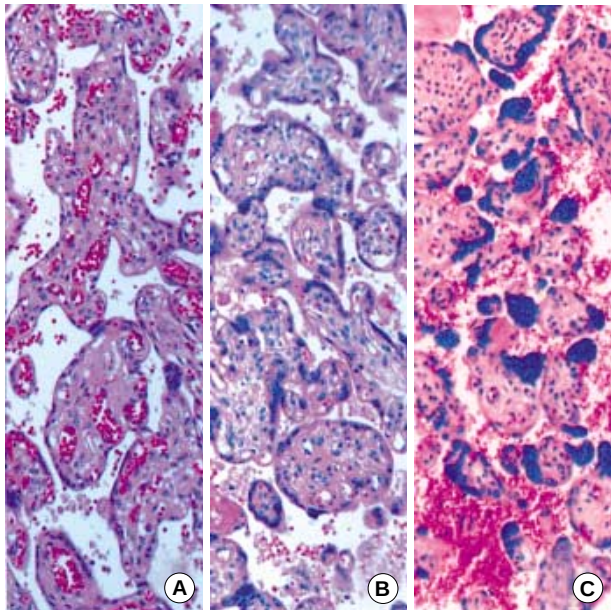

Fig. 2. Increase of syncytiotrophoblastic knots were assessed as normal (A), mildly increased (B), and severely increased (C).

31.1% (14 out of 45 cases) of the IUGR cases compared to 8.3% (2 out of 24 cases) of the AGA cases. Moderate to severe perivillous fibrin deposition (Fig. 3) was more frequently associated with the IUGR group (26.7%, 12 out of 45 cases) than the AGA group (4.2%, 1 out of 24 cases). The incidence of acute chorioamnionitis or acute subchorionitis was significantly higher in the AGA cases rather than in the IUGR cases ($p<0.05$).

Compared with the AGA cases, the combined IUGR cases were histologically characterized by increased incidences of decidual vasculopathy (31.1%, $p=0.001$), multiple and severe infarct ($p=0.001$), villous fibrosis (31.1%, $p=0.039$), increased ST knots (86.7%, $p=0.015$), and higher degree of increased perivillous fibrin deposition ($p<0.05$). There were no significant differences in placental lesions between hypertensive and normotensive IUGR, except decidual vasculopathy (hypertensive IUGR: 46.7% vs. normotensive IUGR: 23.3%) There were no statistically significant differences in incidence for the remaining histologic parameters including fetal thrombotic arteriopathy, avascular villi (Fig. 4), chronic villitis (Fig. 5), and chorangiosis (Fig. 6).

DISCUSSION

IUGR is related to a variety of clinicopathologic factors including maternal, uterine, and fetal factors. Preeminent among the

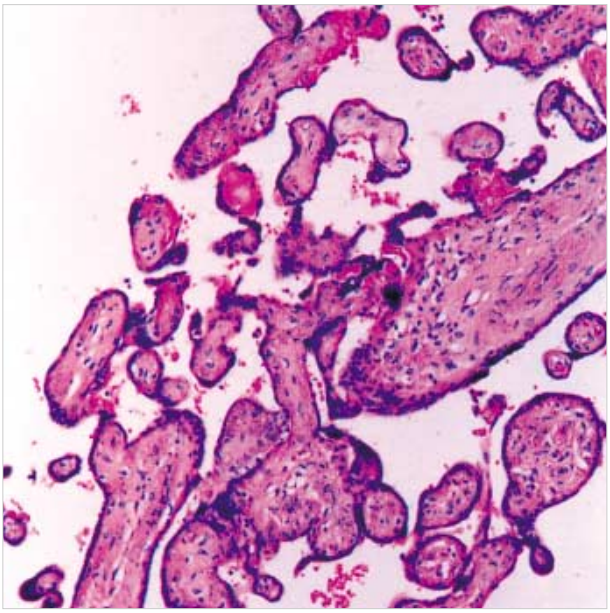

Fig. 4. Avascular villi related to upstream arterial occlusion show bland collagenized stroma.

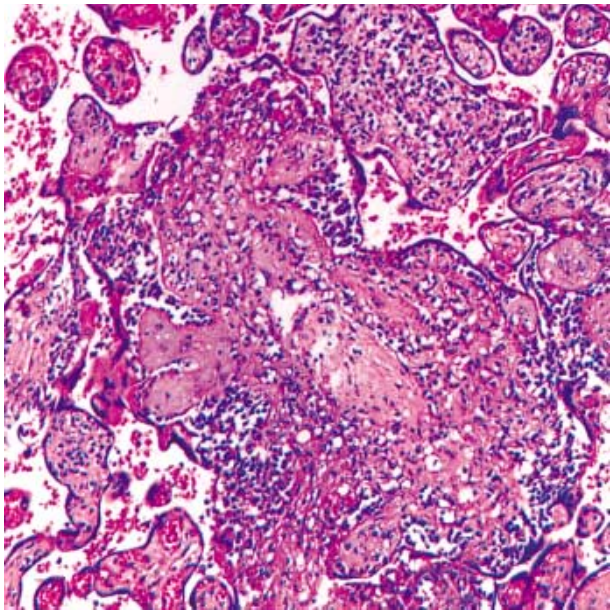

Fig. 5. Chorionic villi shows infiltration of lymphocytes, histiocytes, and plasma cells.

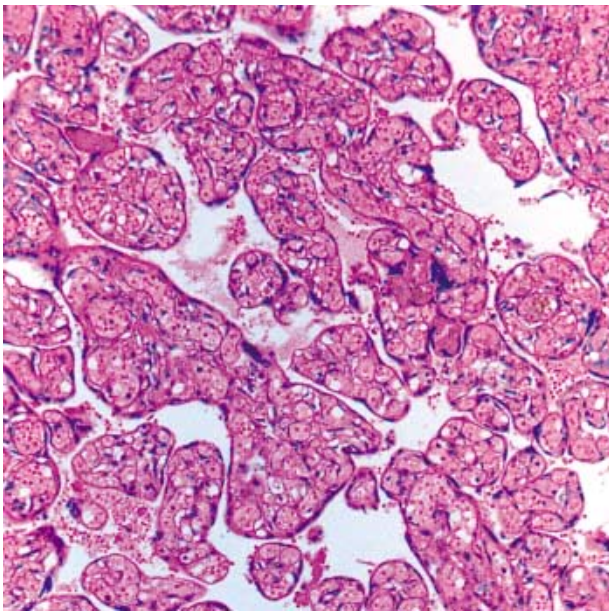

Fig. 6. Villous chorangiosis defined as hypercapillarization of terminal and tertiary stem villi with greater than 10 capillaries per villous cross section.

maternal factors is severe preeclampsia in which the restriction of growth is probably due to the inadequacy of uteroplacental circulation.[1] Although some studies showed that there are no consistent histologic abnormalities in the placentas of IUGR pregnancies,[1] recent studies provide good evidence for the occurrence of distinctive structural and histologic abnormalities in the placentas complicated by IUGR.[9-12]

Macara *et al*.[12] worked on the structural analysis of placental terminal villi from growth-restricted pregnancies with abnormal umbilical artery Doppler waveforms. They found that the terminal villi from the IUGR cases were smaller in diameter than those of the controls, and had increased syncytial nuclei, reduced cytotrophoblastic nuclei, thickened basal lamina, and increased stromal deposition of collagen and laminins. In this study, the IUGR group as a whole was more frequently associated with gross and microscopic abnormalities of the placenta (Table3, 4, and 5). The observed major findings of the placental lesions in the IUGR group were presence of decidual vasculopathy, infarct, increased ST knots, villous fibrosis, and more extensive deposition of perivillous fibrin. The incidence of acute chorioamnionitis was significantly higher in the AGA cases than in the IUGR group. These results may be related to more frequent incidence of vaginal delivery in the AGA cases than in the IUGR cases.

The placentas from pregnancies complicated by IUGR tend to be smaller than those from normal uncomplicated pregnancies.[1,13] In the present study, the placental weights were significantly lower in the IUGR group than in the AGA group, especially in the hypertensive IUGR group. Analysis of placental weight percentiles revealed that only 28.9% of the IUGR cases had placentas greater than those in the 10th percentile, in contrast to the AGA cases which had no cases with placental weights less than those in the 10th percentile.

Since there are certain overt maternal factors that may lead to inadequate fetal growth, we examined placental lesions of IUGR according to the presence or absence of maternal hypertension. In the hypertensive IUGR group of our data set, the observed histolopathologic features were similar to those of previous studies on preeclampsia associated with or without IUGR. These features are presence of decidual vasculopathy, infarct, retroplacental hematoma, ST knots, villous fibrosis, and villous edema.[1,2]

It is interesting to note that the present study demonstrates similarities of placental pathology between normotensive IUGR and hypertensive IUGR. Decidual vasculopathy was considerably found in both IUGR groups, compared to the AGA group ($p<0.005$), although its rate of incidence was higher in the hypertensive IUGR cases (46.7%, 7 out of 15) than in the normotensive IUGR cases (23.3%, 7 out of 30) ($p=0.05$). Decidual vasculopathy was significantly associated with both placental and fetal growth retardation, and was usually found in hypertensive pregnancies.[14,15] However, similar decidual vasculopathy has also been described in the placentas from cases of normotensive IUGR.[10,16]

Uteroplacental vascular insufficiency may compromise placental growth, and it may be related to placental infarction.[1,4] The overall incidences of infarction tends to be increased in placentas from IUGR,[9,10,17,18] although the infarction is small in size in some cases of IUGR. We observed similar incidences of multifocal infarct in normotensive IUGR (30%) and hypertensive IUGR (20%), and these were signifcantly higher than those in AGA (0%, $p<0.01$). Therefore, it would be reasonable to suggest that some normotensive IUGR groups share mechanisms of fetal growth impairment caused by abnormal uteroplacental circulation or immunologic factors.[9,19]

In regard to chronic villitis, Salafia *et al*.[9,20] has emphasized a wide variation in the incidence, dependent upon numbers of sections, with a 30% and 19% incidence of chronic villitis in IUGR and non-IUGR, respectively, at term,[9] and 11.3% and 4.7% incidence in IUGR and AGA, respectively, in another study.[20] Our data revealed 8.9% and 8.3% incidence of chronic villitis in IUGR and AGA cases, respectively. Villitis of unknown etiology (VUE) has long been associated with IUGR though the reported incidence rates have been very variable.[9,21]

Contrary to Redline's[22] emphasis, we observed only a few cases of IUGR with chronic villitis without significant differences in the incidence, compared to AGA. All of our cases with inflammatory lesions were negative for TORCH.

While fetal vessel thrombosis has been reported to be associated with IUGR,[23] we were unable to confirm this in our study. However, we observed groups of avascular villi suggestive of fetal thrombotic arteriopathy more frequently in the IUGR cases than in the AGA cases, although there were no statistically significant differences.

Other less common placental lesions related to IUGR has been described. The first is excessive perivillous fibrin. The cause of increased perivillous fibrin is unknown, but one possible etiologic factor is failure of the mother to expand her intravascular volume appropriately during pregnancy, leading to a low flow state. Our data revealed that IUGR is related to more extensive perivillous fibrin deposition, compared to AGA.

From our study, we concluded that abnormal uteroplacental vasculature and chronic uteroplacental insufficiency, coagulation-related pathology in the uteroplacental, intervillous and/or fetoplacental vasculature, and chronic inflammatory lesions may be the primary disease processes related to the placental pathology of IUGR. Although the cause of IUGR pregnancies is heterogeneous, careful clinicopathologic correlations in individual cases are necessary in the interpretation of placental lesions of IUGR, and the total burden of several placental lesions may be more important than a single histologic feature.

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