Histotopographic Distribution of Placental Inflammation
: Analysis of 22 Cases

Twenty-two placentas were investigated for the presence and patterns of inflammation by extensive examination, and divided into four groups: 1) term vaginal delivery [group I; n=6]; 2) term cesarean section delivery [group II; n=5]; 3) preterm vaginal delivery [group III; n=4], and 4) preterm cesarean section delivery [group IV; n=7]. In group I, all had deciduitis, and choriodeciduitis/chorionitis was present in two cases (33.3%). In group II, four cases (80%) showed deciduitis and/or choriodeciduitis/chorionitis; three of these had intact membranes. In group III, three cases (75%) showed deciduitis, and two had chorionitis. In group IV, three cases (42.9%) showed no evidence of inflammation, three had deciduitis and one had deciduitis/chorioamnionitis. In all groups, membranitis was more severe, confined to the inner and mid segments in general, and deciduitis, choriodeciduitis/chorionitis and chorioamnionitis tended to overlap. The study newly demonstrates major characteristics of placental inflammation: higher prevalence and severity of inflammation in the inner segments of membrane and at the periphery of the placenta. Taking this histotopography into account, it is desirable to take sections from the placental margin, and the current concept of placental inflammation as a surrogate marker of intrauterine infection should be reevaluated.

Key Words : *Placenta; Inflammation; Chorioamnionitis*

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INTRODUCTION

The histopathological diagnosis of placental inflammation is very important because it is associated with increased risk of perinatal morbidity and mortality (1, 2), and it primarily depends on the presence of neutrophilic infiltration of the placenta, membrane, and umbilical cord. Current available data describes that there is a correlation between placental inflammation, represented as chorioamnionitis, and amniotic fluid or placental microbiology. The actual incidence and clinicopathologic significance of acute placental inflammation in pregnancies have not, however, been fully documented (3, 4).

The reported prevalence of placental inflammation shows significant differences ranging 19-81.6% (4, 5), and this can be mainly ascribed to the differences in tissue sampling and criteria of acute inflammation. Biases in tissue sampling may be overcome by taking sections more extensively, and in the present study we tried to examine virtually the entire placenta including chorioamnionic membrane, and umbilical cord by cutting whole placental compartments into sections.

Practical evaluation of the incidence and patterns of placental inflammation was possible using our protocol; the results provided some new information and raised certain questions as to the clinicopathological relevance of the current diagnostic criteria for this condition.

MATERIALS AND METHODS

Collection of materials

A total of 22 placentas was randomly selected at the Department of Pathology, Seoul National University Hospital, during June and July 1995, and the detailed obstetrical histories including mode of delivery, the time lapse between rupture of membrane (ROM) and delivery was retrospectively reviewed. The cases were divided into four groups: 1) term placentas with vaginal delivery [group I; n=6]; 2) term placentas with cesarean section delivery [group II; n=5]; 3) preterm placentas with

vaginal delivery [group III; n=4], and 4) preterm pla-
centas with cesarean section delivery [group IV; n= 7].
After gross examination, the placentas were fixed in 10%
neutral formalin with the entire portion of membrane
fixed in rolls.

Histopathological evaluation of placental inflammation

Formalin-fixed placentas were placed on histotopo-
graphic chart forms, measuring 29.4 × 19.8 cm, in the
Department of Pathology, Seoul National University
Hospital, and whole placentas were sectioned into 2.94
× 1.19 cm-sized pieces. The membrane rolls were sliced
into 1.5 cm- to 2 cm-wide pieces, and sections from the
umbilical cord were taken at 5-cm intervals. The number
of sections ranged from 58 to 148 (mean: 107.0/placen-
ta), and all of the sections were routinely processed and
stained with hematoxylin-eosin. After meticulous light
microscopic examination for the presence of neutrophilic
reaction in the amnion, chorion-decidua, chorionic plate,
and umbilical cord, the degree of inflammation was
graded according to the criteria used by Shurin et al. (6):
0=no infiltrates; 1+=average one to three leukocytes per
high power field (hpf); 2+=mild - four to 15 leukocytes
per hpf; 3+=moderate to severe - more than 15 leuko-
cytes per hpf. The types of inflammation were divided
into deciduitis, choriodeciduitis/chorionitis, chorioamnio-
nitis, and funisitis. Inflammation of the membranes was
categorized into inner (inflammation confined to inner
1/3 of membrane roll), mid (inflammation confined to
mid 1/3 of membrane roll), and outer (inflammation con-
fined to outer 1/3 of membrane roll), and individually
graded. Inflammation of the placenta was divided into
peripheral (inflammation in outer half from center of
placenta) and central (inflammation in inner half from
center of placenta) localization.

RESULTS

Prevalence of placental inflammation

Among 22 cases analyzed, acute deciduitis was the
most common inflammatory feature and was found in 17
cases (77.3%), while choriodeciduitis/chorionitis and cho-
rioamnionitis were present in seven (31.8%) and one
(0.5%) cases, respectively. In group I (n=6), all cases
(100%) were found to have varying degrees of deciduitis,
and choriodeciduitis/chorionitis was present in two cases
(33.3%). Four cases with deciduitis only were delivered
within an hour and nine minutes after rupture of mem-
brane (ROM). In group II (n=5), four cases (80%) show-
ed deciduitis and/or choriodeciduitis/chorionitis; three of

these had intact membranes until cesarean section. In
group III (n=4), three cases (75%) showed deciduitis and
two cases had combined chorionitis. In group IV (n=7),
three cases (42.9%) had no evidence of inflammation, and
two of them had intact membranes until delivery, while
the remaining one was delivered 9 hours and 59 minutes
after rupture of membrane. Among the four cases with
inflammation, three had deciduitis, and deciduitis and
chorioamnionitis were present in one. The number of
cases lacking histopathological inflammation was propor-
tionally greater in group IV than in group I, and funisitis
was not found in all cases.

Histotopographic distribution of placental inflammation

In the membranes including the decidual layer, 14
cases (63.6%) had features of inflammation: group I - 5/7
(71.4%), group II - 3/5 (60%), group III - 3/4 (75%),
and group IV - 3/7 (42.9%). The inflammation in all five
cases of group I was confined to the inner and mid seg-
ments of membrane rolls. Among the three cases with
membranitis in group III, two had inflammation in
whole segments of membrane rolls and in the other,
inflammation was confined to the inner and mid seg-
ments. The majority of cases (5/6; 83.3%) with mem-
branitis in groups II and IV had inflammation in the
inner segments of membrane rolls.

The topographical distribution of placental inflamma-
tion, including that of decidua basalis, showed predomi-
nance in the peripheral compartment of the placenta. The
inflammation was localized at the peripheral part of the
placenta in nine out of 13 cases (69.2%), while only two
cases (15.4%) had centrally localized inflammation. The
remaining two cases (15.4%) had both central and periph-
eral inflammation. The degree of inflammation in general
was more severe at the periphery, and the territories of
deciduitis, choriodeciduitis/chorionitis, and chorioamnio-
nitis in the membrane and the placenta tended to overlap.
Fig. 1 is a schematic overview of the histotopographic dis-
tribution of placental inflammation, and the profiles of
individual cases are summarized in Table 1.

DISCUSSION

The accurate and timely diagnosis of acute placental
inflammation has extreme clinicopathologic significance
because it is known to be associated with intrauterine
infection which usually occurs mainly via an ascending
route. This type of infection is one of the major risk
factors of preterm delivery, perinatal morbidity and mor-
tality (1-4).

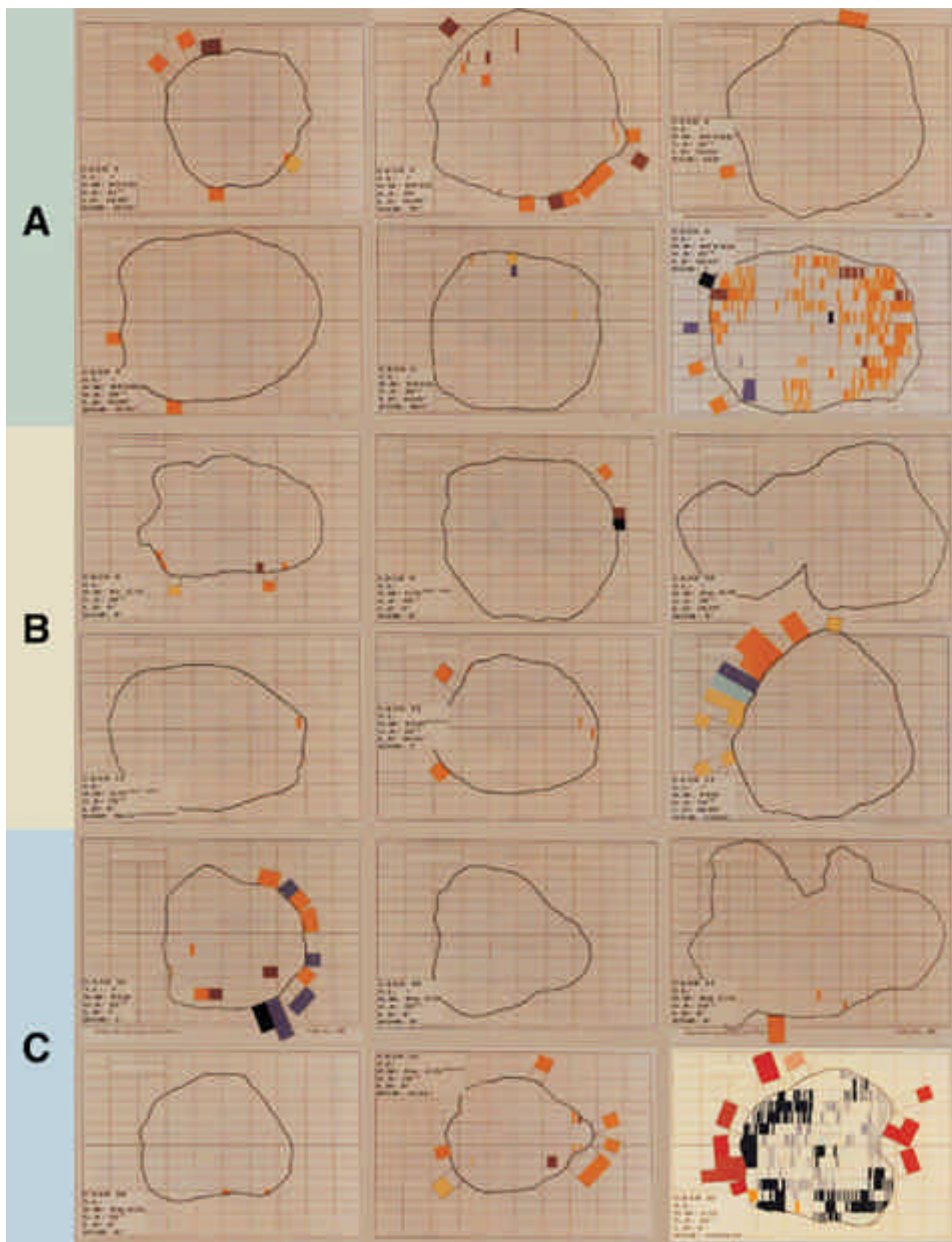Histopathologically, the diagnosis of acute placental

Fig. 1. Schematic presentation of topographical patterns of placental inflammation. The serial case numbers are identical to those in Table 1. The type and the degree of inflammation were represented by color and score (graded from 0-3+), respectively. Cases 7, 12, 18, 19 were devoid of placental inflammation. A, deciduitis; B, choriodeciduitis/chorionitis; C, chorioamnionitis.

Table 1. Summary of clinical profiles of cases (n=22)

Case No.	G.A. (wks)	S.L.	D.M.	L.D.	ROM	Birth weight (g)	A.S.	Remarks
1	41^{+5}	+	NFSD	1:40	0:32	3,240	7-8	
2	38^{+0}	+	NFSD	4:40	0:37	2,850	8-9	
3	39^{+5}	+	NFVED	3:54	1:09	3,280	9-9	
4	39^{+1}	+	NFSD	2:49	0:45	3,270	9-9	
5	40^{+4}	+	NFSD	2:55	9:07	3,150	9-9	
6	42^{+2}	+	NFVED	6:12	?	3,420	8-9	
7	38^{+2}	−	CS	0:00	0:00	3,200	9-9	
8	38^{+4}	−	CS	0:00	0:00	3,740	9-9	
9	38^{+1}	−	CS	0:00	0:00	2,630	9-9	
10	38^{+4}	+	CS	7:34	0:00	2,870	9-9	PIH
11	38^{+4}	−	CS	0:00	9:17	3,080	9-9	PIH
12	34^{+0}	−	PSD	3:20	0:18	1,590	7-8	
13	33^{+0}	−	PSD	9:15	?	1,600	6-8	
14	34^{+6}	+	PSD	6:48	12:31	2,070	7-8	PROM
15	33^{+0}	?	PSD	?	?	1,590	7-7	PIH
16	32^{+0}	+	CS	0:00	0:00	1,030	8-9	PIH, IUGR
17	34^{+6}	−	CS	0:00	0:00	2,150	7-8	PIH
18	31^{+5}	−	CS	0:00	0:00	1,360	2-6	PIH
19	34^{+2}	−	CS	0:00	9:59	2,600	4-8	
20	32^{+1}	−	CS	0:00	0:00	1,140	3-6	PIH
21	30^{+4}	−	CS	0:00	3:14	940	2-5	PIH, IUGR
22	33^{+1}	−	CS	0:00	64:16	1,960	8-8	PROM

G.A., gestational age; S.L, spontaneous labor; D.M., delivery mode; L.D., labor duration; ROM, duration between rupture of membrane and delivery; A.S., Apgar score; NFSD, normal fullterm spontaneous delivery; NFVED, normal fullterm vacuum extracted delivery; PSD, preterm spontaneous delivery; CS, cesarean section; PIH, pregnancy-induced hypertension; PROM, premature rupture of membrane; IUGR, intrauterine growth retardation.

inflammation is based on neutrophilic infiltration of the placental compartments, and even the collection of a few neutrophils is accepted as evidence of placental inflammation (6, 7). Furthermore, the histopathological diagnosis of inflammation is almost always dependent on the observation of relatively few representative samples taken, according to standard protocol, from the placenta, membrane including rupture site, and umbilical cord. Although this is the best choice (8), it seems that adequate diagnosis may be impossible if the inflammatory process is localized or shows regional differences. For example, if the distribution of inflammation is localized in the early phase of acute inflammation, the sections from distant parts of the placenta will be free of inflammation. In this context, the differences in the prevalence of placental inflammation among previous studies may be partially due to different modes of tissue sampling, along with different histopathological criteria of inflammation (1, 3-7).

In the present study, we tried to estimate the real incidence and to analyze the topographical distribution of placental inflammation by extensive tissue sampling and meticulous examination, and thereby reevaluate the clinicopathologic significance and limitations of conven-

tional histopathological diagnosis of placental inflammation based on current diagnostic criteria and establish additional guidelines for histopathological interpretation.

Our data clearly demonstrates that histopathological inflammation is present in virtually all of the placentas delivered at term, despite the mode of delivery, and that the incidence of inflammation seems to be lower in the preterm placentas especially in the cases delivered by cesarean section (group IV). Due to the limited number of cases, it does not, however, seem to be appropriate to attach statistical significance. The presence of acute inflammation in term placentas of babies with uneventful perinatal outcome raised a basic question as to the clinicopathological significance of minimal placental inflammation, and we supposed that the current histopathological criteria of placental inflammation may be too strict, as well as hypersensitive. Therefore, we also believe that the current concept of minimal histopathological placental inflammation as a surrogate marker of significant intrauterine infection should be reevaluated.

From the histotopographical point of view, our study newly documented two major characteristics of placental inflammation. One was the higher prevalence and severity of inflammation in the inner segments (proximal por-

tions) of the chorioamnionic membrane, which absolutely contradicts previous descriptions stating that inflammation of the membrane is usually identified around rupture sites (7, 9); the other was the higher prevalence and severity of inflammation at the periphery of the placenta. These findings were consistent in all groups. Our data strongly suggests that the propagation of placental inflammation may start from the marginal portion of the placenta and proximal parts of the membrane, and does not support the view that the infectious process may be a cause of membrane rupture, especially in preterm deliveries (10). Taking this histotopographical constitution of placental inflammation into account, it is desirable, for effective diagnosis of inflammation, to obtain two to four sections from the marginal portion of the placenta.

Intrauterine infection is a major cause of perinatal morbidity and it is certain that placental inflammation is a sign of intrauterine infection associated with preterm labor (11-14). However, for the histopathological diagnosis to be of clinicopathological relevance, more understanding of the significance of leukocytic infiltration of the placenta should be preceded by more future systematic studies. Among pathologists, extremely sensitive diagnostic criteria of placental inflammation might have been the major cause of discrepancies in histopathological inflammation, bacteriologic studies, and clinical features of intraamniotic infection (15).

In the present study, the majority of term placentas with uneventful perinatal outcome had varying degrees of placental inflammation and we think that cases showing only focal collections of few (one to three) neutrophils do not deserve to be described as placental inflammation. Group II in our study, who were delivered by uncomplicated cesarean section, showed features of choriodeciduitis/chorionitis in two out of five cases. The application of more strict diagnostic criteria will be one of the solutions to the adequate interpretation of placental inflammation; Dong et al. (4) have already pointed out the strong correlation between rather severe placental inflammation and amniotic fluid microbiology.

We are not sure whether the phenomenon of acute deciduitis in the present study resulted from ascending infection or was a physiologic phenomenon related to progesterone withdrawal, as previously suggested (7, 16). Acute deciduitis alone has been excluded from placental inflammation in previous studies (17, 18), but the obvious overlapping in the distribution of deciduitis, choriodeciduitis/chorionitis, and chorioamnionitis strongly suggests that deciduitis is a precursor lesion of choriodeciduitis/chorionitis and chorioamnionitis. The major problem of the present study is the limited number of cases, but we believe that the information will make a sub-

stantial contribution to future studies dealing with pathologic aspects of placental inflammation.

Acknowledgments

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