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Diagnosis of Placental Abruption: Relationship between Clinical and Histopathological Findings

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Abstract

Objective—We evaluated the extent to which histologic lesions bearing a diagnosis of abruption conform to a diagnosis based on established clinical criteria. We further examined the profile of chronic and acute histologic lesions associated with clinical abruption.

Methods—Data from the New Jersey-Placental Abruption Study – a multi-center, case-control study – were utilized to compare the clinical and histologic criteria for abruption. The study was based on 162 women with clinically diagnosed abruption and 173 controls. We examined the concordance between clinical indicators for abruption with those of a histopathological diagnosis. The clinical criteria for a diagnosis of abruption included (i) evidence of retroplacental clot(s); (ii) abruption diagnosed on prenatal ultrasound; or (iii) vaginal bleeding accompanied by nonreassuring fetal status or uterine hypertonicity. The pathological criteria for abruption diagnosis included hematoma, fibrin deposition, compressed villi, and hemosiderin-laden histiocytes in cases with older hematomas. Acute lesions included chorioamnionitis, funisitis, acute deciduitis, meconium stained membranes, villous stromal hemorrhage, and villous edema. Chronic lesions included chronic deciduitis, decidual necrosis, decidual vasculopathy, placental infarctions, villous maldevelopment (delayed or accelerated maturation), hemosiderin deposition, intervillous thrombus, and chronic villitis.

Results—Of clinically diagnosed cases, the sensitivity and specificity for a histologic confirmation of abruption were 30.2% and 100%, respectively. Presence of retroplacental clots remained the single most common finding (77.1%) among clinically diagnosed cases. Among the acute lesions, chorioamnionitis and funisitis were associated with abruption. The only chronic histologic lesion associated with abruption was placental infarctions.

Conclusions—The concordance between clinical and pathologic criteria for abruption diagnosis is poor. The criteria for diagnosing a clinical abruption should include sonographic visualization of

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abruption, evidence of retroplacental clots, or vaginal bleeding accompanied by nonreassuring fetal status or uterine hypertonicity.

Keywords

Placental abruption; histopathologic lesions; chronic etiology; villous maturation; villous dysmaturity; infarctions; abruption diagnosis

Introduction

Placental abruption, the premature separation of the placenta, is a serious obstetric complication that occurs in about 1–2 per 100 pregnancies (1–3). Over half of all pregnancies complicated by abruption deliver preterm (4–6), and abruption is associated with an array of adverse maternal and fetal outcomes (7–9). The etiology of placental abruption remains speculative but is thought to be the consequence of abnormal trophoblast invasion leading to rupture of the spiral arteries and premature separation of the placenta (10).

Despite being an important obstetrical condition, placental abruption lacks a unified diagnostic clinical criterion. Histologic evidence supporting a chronic process that frequently accompanies placental abruption has led researchers to speculate that the condition is the end-result of an underlying chronic process with origins very early in pregnancy, and perhaps even extending to the time of implantation (11,12). In the presence of vaginal bleeding accompanied by abdominal pain, uterine contractions, or uterine tenderness (13), placental abruption is first considered in the differential clinical diagnosis. At delivery, old or freshly adherent blood clots are diagnostic of abruption. Some of these placentas, but not all, may have histologic features of placental abruption. Moreover, there have been cases of women diagnosed with placental abruption based on histological markers that showed a clinically unremarkable obstetrical course and outcome (14).

Given these uncertainties surrounding the diagnosis of placental abruption, we sought to determine the concordance between a clinical and histologic diagnosis of placental abruption. Additionally, we evaluated associations between acute and chronic placental lesions and abruption to determine if findings from the placenta might provide some insights as to whether placental abruption is the result of an acute event or a chronic process.

Material and Methods

New Jersey—Placental Abruption Study (NJ-PAS)

Women with a clinically diagnosed placental abruption were recruited from either Saint Peters University Hospital (SPUH) or Robert Wood Johnson University Hospital (RWJUH) in New Brunswick, NJ. Subjects were recruited between August 2002 and June 2004 at SPUH and between July 2003 and June 2007 at RWJUH. Placental abruption cases were matched to controls based on their race/ethnicity and parity to those who experienced an otherwise normal delivery. Because the original study was designed to examine thrombophilic markers in relation to placental abruption, abruption cases and controls were not matched on gestational age at delivery. Further details of the NJ-PAS are described in detail elsewhere (15–17).

The study was approved by the institutional review boards of both hospitals as well as that of UMDNJ-Robert Wood Johnson Medical School.

Placental abruption cases and controls

Women with a confirmed or suspected clinical diagnosis of placental abruption were eligible for recruitment as potential cases. Placental abruption cases, or women suspected to have

experienced an abruption by the delivering physician, were regarded as true cases if they satisfied at least one of the following 3 specific clinical criteria: (i) patients presenting with classical signs of painful vaginal bleeding accompanied by at least one of the following: nonreassuring fetal status, severe abdominal pain, tetanic uterine contractions, or uterine hypertonicity; (ii) the freshly delivered placenta showing evidence of clinically significant retroplacental bleeding or clot(s); or (iii) placental abruption diagnosed on prenatal ultrasound (18).

Vaginal bleeding was categorized as those who presented with bleeding upon admission to the hospital, had episodes of bleeding immediately prior to the onset of labor, or had excessive bleeding during labor. Nonreassuring fetal status was classified when either bradycardia or tachycardia was documented, (19) a charted steep decrease in fetal heart rate was seen on tracings, or otherwise documented by physician. Bradycardia and tachycardia were defined as baseline heart rate less than 110 and greater than 160 beats per minute, respectively (20).

Women whose pregnancies were not complicated by placental abruption were recruited as controls, and were matched to abruption cases on race/ethnicity and parity. Controls were identified daily using hospital medical records and in the absence of any clinical documentation of abruption, a woman with whom there was a case match was approached for consent. All placentas (cases and controls) for consenting women were then sent to pathology. A microscopic slide and 1-inch piece of the umbilical cord were then collected for our study. All placental samples were stored in a frozen state until examined by pathologist. Women diagnosed with placenta previa among cases or controls were excluded. Additionally, those diagnosed with placental abruption in a previous pregnancy were excluded from the eligible pool of controls. If a woman had a past abruption, they were still considered case candidates if they had a subsequent abruption during our study period.

Pathological diagnosis of placental abruption

After delivery, the entire placenta was submitted to the pathologist for gross examination, optimal sampling, staining and microscopic examination. Optimal sampling techniques included 3 placental blocks, one with 2 sections of umbilical cord and a roll of extraplacental membranes, one block each of fetal and maternal surfaces; when gross lesions were identified, additional sections, up to 3 blocks, were submitted. All gross and histologic lesions were scored on a standardized data sheet, and the perinatal pathologist at each hospital was blinded to the case-control status.

Gross examination of the placentas was performed by a trained pathology assistant and supervised by the pathologist. Placentas were examined in the fresh state. Histopathological evaluation included both gross and microscopic findings of the placenta, umbilical cord, and membranes. A diagnosis of placental abruption was made by the pathologist based on a thorough macroscopic and microscopic examination of the placenta. Macroscopic evidence of abruption included retroplacental hemorrhage, indentation or hematoma with or without recent or old infarctions. On microscopic examination, we looked for villous infarctions associated with decidual destruction, hemorrhage and adjacent increased syncytiotrophoblast knotting (21). In cases of older abruption (i.e., a few days' duration) a search for foci of villous compression due to hematoma and evidence of bleeding of 2–3 days duration such as pigmented histiocytes (22) (hemosiderin-laden macrophages), was also performed. It is observed that in old and small abruptions, the only observations may be minor color changes and infarcts. Although approximate estimates can be given regarding the age of retroplacental clots, exact figures cannot be given. Villous edema, although a fairly nonspecific change, is a consistent finding in cases of placental abruption (23). Due the nonspecific nature of this histologic finding, we did not score villous edema.

Histological lesions

Evidence from previous studies collectively suggests that placental abruption is the manifestation of clinical events that likely have at least 2 distinct causative pathways: (i) acute-inflammation-associated conditions; and (ii) chronic processes including vascular dysfunction and chronic inflammation. Therefore histologic lesions were scored and grouped as acute or chronic histologic lesions (4,5,24–26). Acute histologic lesions included chorioamnionitis, acute deciduitis, funisitis, villous edema, villous stromal hemorrhage, and meconium stained membranes associated with amnion necrosis and pigmented macrophages. Chorioamnionitis was defined by the presence of inflammatory infiltrates of neutrophils at two or more sites on the chorionic plate and extra-placental membranes. It was classified into one of four grades: none, mild, moderate and severe. Mild chorioamnionitis was defined by the presence of few scattered (5–10/high power field) neutrophils in the subchorionic space and adjacent chorion; moderate was defined by many (11–30/high powered field) neutrophils in the lower half of the chorionic plate; and severe by dense infiltrates of neutrophils (>30/high powered field) throughout the chorionic plate into the amnion (27). Funisitis was identified when neutrophils infiltrated the umbilical cord stroma (Wharton's jelly). Villous stromal hemorrhage was identified if there were erythrocytes within the stroma of chorionic villi.

Chronic lesions included chronic deciduitis (lymphocytes with or without plasma cells), maternal floor decidual necrosis, villitis, decidual vasculopathy (specifically, in the vessels of the extraplacental membrane roll), placental infarction, intervillous thrombosis, villous mal-development, and hemosiderin deposition. Villous mal-development included the findings of delayed maturation (increased villous size, increase in stromal cells and decreased syncytial knotting) and accelerated villous maturation (small and slender villi with reduced branching, and increased syncytial knotting). Decidual vasculopathy comprised of muscular thickening, decidual thrombosis or atherosclerosis occurring within the vessels contained in the extraplacental membrane roll.

Statistical analysis

Frequencies of acute and chronic lesions were compared in 2 sets of analysis. In the first analysis, we compared the distribution of lesions between abruption cases and controls; in the second analysis restricted to abruption cases, we compared lesions between women that had a confirmed and unconfirmed abruption based on histologic criteria. Unadjusted odds ratio (OR) and 95% confidence interval were determined to evaluate the strength of association in both sets of analysis. Adjusted odds ratio and 95% confidence interval was estimated from multivariable logistic regression models after adjusting for potential confounders (listed in Table 1).

All statistical tests were two-tailed, and statistical analysis was done using SAS (version 9.1; SAS Institute, Cary, NC).

Results

Of a total of 424 enrolled patients, placental histological examination was completed in 88.2% (n=374) patients. The study was restricted to those with completed placental examination and women that delivered a singleton birth, leaving a total of 162 abruption cases and 173 controls. One hundred and seventeen patients were enrolled at RWJUH (60% of abruption cases) and 218 patients were enrolled at SPUH (42% of abruption cases). Among the 162 clinically diagnosed abruption cases, 30.2% (n=49) were also “confirmed” as placental abruption based on gross or histological findings. Demographic characteristics of cases and controls are shown in Table 1.

Diagnosis of placental abruption

The most common indication leading to a clinical diagnosis of abruption (Table 2) was evidence of retroplacental clot(s) or bleeding (77.1%), followed by vaginal bleeding with uterine hypertonicity (27.8%) and by vaginal bleeding with nonreassuring fetal status (16.1%).

Histologic lesions in placental abruption cases and controls

The distributions of acute histologic lesions between cases and controls, as well as between histologically confirmed and unconfirmed abruption cases, are described in Table 3. Acute lesions that were associated with abruption included chorioamnionitis and funisitis (funisitis was statistically insignificant). In a comparison between cases with and without histologic confirmation of abruption, none of the acute lesions was significantly associated with abruption.

The distributions of chronic lesions in abruption cases and controls are shown in Table 4. There was a greater frequency of placental infarctions among abruption cases (29.0%) than controls (13.3%), and they were significantly associated with abruption. A comparison between histologically confirmed versus unconfirmed abruption cases revealed a significant association of both decidual vasculopathy and placental infarctions.

Discussion

Despite extensive research, the etiology of placental abruption remains speculative, perhaps, to a large extent, because of the lack of appropriate diagnostic criteria. Our study reveals several important and clinically relevant findings regarding placental abruption: (i) the diagnosis of abruption should be based on clinical criteria, since an examination of the placenta for confirmational purposes is not sensitive; (ii) the diagnostic criteria should include the presence of retroplacental clot(s) or bleeding, ultrasound diagnosis, or vaginal bleeding accompanied by either nonreassuring fetal status or uterine hypertonicity; and (iii) the profile of acute and chronic histologic lesions associated with placental abruption remains poorly understood.

Clinical indicators for placental abruption

Conditions most indicative of a clinically diagnosed placental abruption are vaginal bleeding accompanied by nonreassuring fetal status, ultrasound diagnosis and retroplacental clots or vaginal bleeding. Indicators most consistent with a positive diagnosis of placental abruption upon histological examination included retroplacental clot or bleeding and ultrasound diagnosis.

Clinical indicators, such as nonreassuring fetal status in the presence of vaginal bleeding, as well as retroplacental clots/bleeding may be important markers for a clinical diagnosis of placental abruption. These clinical indicators, however, are of little value for the obstetrical management of pregnancies at impending risk for abruption. An increase in definitive diagnosis may lead to better preparation for delivery complications. Ultrasound diagnosis continues to be a weak marker for placental abruption in our study (14.8% for clinical diagnosis), although previous studies have suggested the value of prenatal sonography in diagnosing placental abruption (28). Recent studies show evidence that the etiology of abruption is more of a chronic inflammatory process than an acute event (4,29). Evidence in support of this is, however, weak in our study.

Histologic lesions in placental abruption cases and controls

Our analysis of histologic lesions of the placenta, cord, and membranes, sought to help determine the relationship between a clinical diagnosis of placental abruption cases and controls. The chief findings of our study were (i) chronic lesions were implicated in 100% of

histologically confirmed abruptions; (ii) the only chronic lesions significantly involved in the pathophysiologic process of abruption included placental infarctions and decidual vasculopathy; and (iii) only a third of clinically-diagnosed abruption cases were confirmed by gross and histopathologic examination. Placental abruption most often presents clinically as an acute event. However, it has frequently been cited that abruption is a slow, chronic process, sometimes visualized sonographically for evidence of retroplacental hemorrhage or hematoma (23,30,31). Infarctions, when present, are likely to cause underperfusion to the uteroplacental bed (26), which, over an extended period, may result in increased placental resistance. This, in turn, is likely to lead to destruction of blood vessels and extend to feto-maternal bleeding (32) and ultimately manifesting as placental abruption.

Limitations and biases of the data

Limitations of our study include observation bias. Since patients were enrolled from several different obstetrical practices, there may be differences in the level of subjectivity associated with diagnosis and chart documentation. This may increase or decrease the prevalence of certain indicators for placental abruption. Furthermore, each hospital employed its own pathologist to evaluate the placentas and score the lesions, which may introduce some classification bias. Because data were abstracted from medical charts, there is a possibility that information was transcribed incompletely, or in error, concerning indications during delivery. Since data abstractors were not blinded to the case-control status, this may have led to a bias in differential ascertainment. If present, this may have led to a bias in association away from the null. One dilemma arises from our low concordance rate between histology and clinical diagnoses: the low concordance rate leaves room for speculation as to whether observation of these placentas for a confirmatory diagnosis of abruption may not be an optimal allocation of financial resources and time.

Abruption cases were not matched to controls based on gestational age at delivery. As seen in Table 1, a higher frequency of preterm delivery was seen among cases than controls. While appropriate, some of our results may be confounded by the well known increased frequency of histological abnormalities among preterm deliveries and preeclampsia. However, due to our small sample size of cases delivering at term (≥ 37 weeks) and of preeclampsia, we were unable to further examine histologic lesions within sub-groups. Further studies are needed to corroborate our findings, and specifically to examine the profile of histologic lesions associated with placental abruption based on preterm birth status and preeclampsia.

Strengths of the study

Benefits of this study include an overall moderately large sample size that was recruited over a five year period. Background and pregnancy data were available and forwarded for $>90\%$ of patients; and comparison of questionnaire data in relation to medical chart data yields a moderately low recall bias among patients (data not shown). Additionally, all blood samples (maternal and cord) were gathered within 3 days of delivery, ensuring a sample that is fresh to the placental abruption (or lack thereof.) This study had the benefit of two modes of patient capture. The medical team within the hospital would contact study team of abruption, in addition to the daily review of hospital charts by study team nurse. This method allowed for the capture of most study participants. Lastly, pathologists were blinded to case-control status, thereby potentially reducing classification bias among all histology record reports.

Conclusions

This study suggests that (i) the concordance between the clinical and pathological diagnosis of placental abruption is poor; (ii) clinical diagnosis for abruption should include one or more of the following: retroplacental bleeding or clot(s), sonographic visualization of abruption, or

painful vaginal bleeding accompanied by nonreassuring fetal status or uterine hypertonicity; and (iii) a vast majority of placental abruption cases appears to have a long-standing chronic etiology. These findings may serve important roles in the diagnosis and appropriate clinical management of women diagnosed with placental abruption.

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APPENDIX

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Table 1

Demographic characteristics of clinically diagnosed placental abruption cases and controls

Maternal characteristics	Abruption cases (n=162)		Controls (n=173)	
	n	%	n	%
Maternal age (years)				
<20	8	4.9	11	6.4
20–24	27	16.7	23	13.3
25–29	36	22.2	36	20.8
30–34	49	30.3	55	31.8
≥35	42	25.9	48	27.7
Parity				
Parity 0	54	33.3	61	35.3
Parity 1	59	36.4	61	35.3
Parity ≥2	49	30.3	51	29.5
Gestational age (weeks)				
<25	12	7.4	2	1.2
25–35	94	58.0	19	11.0
≥37	56	34.6	152	87.9
Maternal race/ethnicity				
Caucasian	56	34.6	67	38.7
Hispanic	55	34.0	53	30.6
African American	26	16.1	28	16.2
Other	25	15.4	25	14.5
Maternal education (years)				
<9	14	8.6	15	8.7
9–12	62	38.3	48	27.7
13–15	67	41.4	75	43.4
≥16	20	12.4	35	20.2
Prepregnancy BMI				
Underweight	35	21.6	32	18.5
Normal	75	46.3	81	46.8
Overweight	32	19.8	33	19.1
Obese	20	12.4	27	15.6
Maternal smoking	23	14.2	18	10.4
Alcohol use	1	0.6	8	4.6
Preeclampsia	23	14.2	2	1.2

BMI, body-mass index

Alcohol use = 1–7 drinks per week

Table 2

Criteria for the clinical diagnosis of placental abruption

Indicators for a clinical diagnosis of placental abruption	Clinically diagnosed placental abruption cases			
	All clinical cases (n=162) n (%)	Pathology confirmed* (n=49) n (%)	Pathology unconfirmed** (n=113) n (%)	Controls (n=173) n (%)
Retroplacental clot(s)/hemorrhage	125 (77.1)	42 (85.7)	83 (73.5)	—
Ultrasound diagnosis	24 (14.8)	11 (22.5)	13 (11.5)	—
Vaginal bleeding + nonreassuring fetal status	45 (16.1)	8 (16.3)	37 (37.7)	—
Vaginal bleeding + uterine hypertonicity	16 (27.8)	5 (10.2)	11 (9.7)	—
Vaginal bleeding only	0	0	0	1 (0.6)
No indications present	0	0	0	172 (99.4)

* Clinically diagnosed abruption cases also confirmed on placental pathology

** Clinically diagnosed abruption cases not confirmed as placental abruption on placental pathology

Table 3

Associations between acute histologic lesions and placental abruption cases and controls, and between histologically confirmed and unconfirmed abruption cases

Acute histologic lesions	Clinically diagnosed abruption cases			Adjusted odds ratio (95% CI)	
	All clinical cases (n=162)	Pathology confirmed* (n=49)	Pathology unconfirmed** (n=113)	All clinical cases vs controls† (n=173)	Pathology confirmed vs unconfirmed‡
Chorioamnionitis (%)	19.8	16.3	21.2	3.0 (1.4, 6.1)	0.8 (0.3, 2.0)
Funisitis (%)	4.3	6.1	3.5	2.3 (0.5, 9.6)	2.0 (0.4, 10.7)
Acute deciduitis (%)	0.6	0.0	0.9	0.3 (0.0, 2.5)	—‡
Meconium (%)	11.1	12.2	10.6	0.5 (0.3, 0.9)	0.7 (0.3, 2.2)
Villous stromal hemorrhage (%)	0.0	0.0	0.0	—	—
Villous edema (%)	92.5	91.8	94.7	0.3 (0.1, 0.9)	0.8 (0.2, 2.7)
At least 1 lesion	96.9	97.8	96.5	—	—

* Clinically diagnosed abruption cases also confirmed on placental pathology

** Clinically diagnosed abruption cases not confirmed as placental abruption on placental pathology

† Odds ratios are adjusted for maternal age

‡ Adjusted odds ratio not reported due to insufficient sample size

Table 4

Associations between chronic histologic lesions and placental abruption cases and controls, and between histologically confirmed and unconfirmed abruption cases

Chronic histologic lesions	Clinically diagnosed abruption cases			Adjusted odds ratio (95% CI)		
	All clinical cases (n=162)	Pathology confirmed* (n=49)	Pathology unconfirmed** (n=113)	Controls (n=173)	All clinical cases vs controls†	Pathology confirmed vs unconfirmed‡
Chronic deciduitis	97.5	98.0	97.4	96.5	1.4 (0.4, 4.9)	1.5 (0.2, 15.2)
Decidual necrosis	2.5	4.1	1.8	4.1	0.6 (0.2, 2.2)	2.1 (0.3, 15.6)
Decidual vasculopathy‡	19.8	30.6	15.0	13.3	1.6 (0.9, 3.0)	2.5 (1.1, 5.9)
Placental infarctions	29.0	49.0	20.4	13.3	3.1 (1.7, 5.6)	3.9 (1.9, 8.4)
Advanced maturation	9.3	6.1	10.6	5.8	1.9 (0.8, 4.6)	0.5 (0.1, 1.8)
Dysmaturation	73.5	80.0	70.8	80.4	0.6 (0.4, 1.0)	1.9 (0.8, 4.3)
Hemosiderin deposition	1.2	0.0	1.8	1.2	1.1 (0.2, 8.0)	—
Intervillous thrombus††	5.6	8.1	4.4	19.1	0.3 (0.1, 0.6)	1.83 (0.5, 7.2)
Villitis	0.0	0.0	0.0	0.6	—	—
At least 1 lesion	98.7	100	98.2	100	—	—

* Clinically diagnosed abruption cases also confirmed on placental pathology

** Clinically diagnosed abruption cases not confirmed as placental abruption on placental pathology

† Odds ratios are adjusted for maternal age

‡ Decidual vasculopathy includes muscular thickening and atherosclerosis

†† Intervillous thrombus includes lesions associated with feto-maternal hemorrhage, and large placentas of diabetes or erythroblastosis