—Report on Experiments and Clinical Cases—

Fetal Heart Rate Monitoring as a Predictor of Histopathologic Chorioamnionitis in the Third Trimester

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Abstract

Chorioamnionitis (CAM) has been recognized as a common cause of neonatal morbidity and mortality. The effect of CAM on fetal heart rate (FHR) remains unclear. The purpose of this descriptive retrospective study was to evaluate the clinical significance of the FHR pattern in cases that involved delivery during the third trimester and the diagnosis of histopathological CAM. The study group consisted of 65 singleton live births delivered at 28 to 41 weeks' gestation from January 2003 through December 2005 in which histopathological CAM was diagnosed at the Nippon Medical School Tama Nagayama Hospital. We reviewed the cases using medical records and examined FHR data and the severity of histopathological CAM. The rate of tachycardia according to the severity of CAM was as follows: 3.0% (1 of 33 cases) in intervillositis, 12.5% (3 of 24 cases) in chorionitis, 37.5% (3 of 8 cases) in CAM (in a narrow sense); however, this tendency had no statistical significance. Baseline variability and decelerations were not correlated with the severity of histopathological CAM. Maternal fever exceeded 38.0℃ in only 3 cases, and 1 fetus had exhibited an abnormal FHR pattern. The present study suggests that FHR monitoring is not a reliable means of diagnosing histopathological CAM, because the FHR pattern was normal in most cases of histopathological CAM.

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Key words: chorioamnionitis, fetal heart rate monitoring

Introduction

Chorioamnionitis (CAM), associated with a fetal systemic inflammatory response syndrome, has been recognized as a common cause of neonatal morbidity and mortality[1,2]. CAM plays a role in the development of brain injury, particularly white matter damage due to elevated circulating inflammatory cytokines and the coexistence of inflammatory and thrombotic lesions[3]. Clinical CAM is diagnosed when maternal fever is associated with the signs and symptoms of intrauterine inflammation (i.e., foul-smelling discharge and uterine tenderness) and laboratory evidence of maternal leukocytosis[4]. A large percentage of cases of histopathological CAM are subclinical, and a satisfactory noninvasive antenatal marker that would aid in the diagnosis of

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these cases during pregnancy is not yet available[2].

Although, fetal heart rate (FHR) monitoring has been used in the management of labor and delivery, the effect of CAM on the FHR remains unclear[5–11]. The purpose of this study was to evaluate the clinical significance of the FHR pattern in cases of third-trimester delivery and subsequent diagnosis of histopathological CAM.

Materials and Methods

This study was a descriptive retrospective study. At the Nippon Medical School Tama Nagayama Hospital, placental pathological examination was performed in cases of suspected perinatal risk, such as clinical CAM, placental abruption, pregnancy-induced hypertension, intrauterine growth retardation, and multiple pregnancy. A total of 168 placental examinations were performed from January 2003 through December 2005. After cases of birth at less than 28 week's gestation, multiple pregnancy, and intrauterine fetal death were excluded, 105 cases remained. Histological CAM was diagnosed in 65 of these cases, which comprised the present study group.

We reviewed the cases using medical records and examined FHR data and the severity of histological CAM. Moreover, we reviewed clinical diagnoses, delivery modes, maternal findings (body temperature, maternal white blood cell [WBC] count, and maternal C-reactive protein [CRP] level), and neonatal findings (birth weight, umbilical arterial pH [UApH], and Apgar scores at 1 and 5 minutes). This study was approved by the institutional review board of the Nippon Medical School Tama Nagayama Hospital.

Recording of the FHR was performed for all fetuses as part of routine obstetric care. The FHR monitoring was performed continuously until delivery, once active labor occurred, or until emergency cesarean section was started. The FHR patterns were interpreted according to the guidelines of the National Institute of Child Health and Human Development[12]. Variable decelerations were defined as decreases in FHR of 15 beats per minute (bpm) from baseline lasting 15 seconds to 2 minutes. Late decelerations were defined as transient but repetitive decreases in FHR appearing late in the contraction phase. Prolonged decelerations were defined as decreases in FHR of 15 bpm from baseline lasting 2 to 10 minutes. Normal FHR variability was defined changes of 6 to 25 bpm (a long cyclicity); changes outside this range were defined as abnormal FHR variability. Bradycardia was defined as a FHR of <110 bpm for at least 10 minutes, and tachycardia was defined as rate of >160 bpm for at least 10 minutes. In this study, we analyzed 40 minutes of FHR monitoring charts before the second stage of labor or the start of cesarean section. Decelerations were classified into two groups: negative and positive. The positive group included late, variable, and prolonged decelerations. Late and variable decelerations were defined as recurrent if they occurred with more than 50% of uterine contractions. If one or more prolonged decelerations occurred during pregnancy and delivery, we defined them as prolonged decelerations.

Microscopic histopathological analysis of the placentas was performed after delivery according to Blanc's criteria[13]. The severity of CAM, i.e., inflammation of the placental surface, was determined via the degree of maternal polymorphonuclear lymphocyte infiltration into either the subchorionic space (intervillositis: stage 1), the intervillous space (chorionitis: stage 2), or the amniotic cavity (CAM in a narrow sense: stage 3).

Continuous data are expressed as the mean and standard deviation. Comparisons were performed with Student's *t*-test for continuous data or the likelihood ratio method for group data. Differences with a P value of less than 0.05 were considered to be statistically significant.

Results

Of the 65 study cases, 33, 24, and 8 cases were diagnosed as stage 1, stage 2, and stage 3 histological CAM, respectively. The characteristics of subjects are shown in **Table 1**. The mean maternal age was 32.3 ± 4.8 years, and the mean gestational age at delivery was 37.5 ± 3.0 weeks.

Table 1 Characteristics of Study Subjects

		CAM stage 1[a] (n=33)	CAM stage 2[b] (n=24)	CAM stage 3[c] (n=8)	Total (n=65)
Age		32.3 ± 4.9	31.8 ± 5.1	31.1 ± 3.6	32.3 ± 4.8
Primigravida		13 (39.4%)	11 (45.8%)	2 (25.0%)	26 (40.0%)
Primipara		19 (57.6%)	13 (54.2%)	3 (37.5%)	35 (53.8%)
Gestational age (week)		37.8 ± 2.5	37 ± 3.5	37.3 ± 3.3	37.5 ± 3.0
Birth weight		2,553 ± 646.1	2,397.3 ± 660.1	2,255.9 ± 591.8	2,455.7 ± 633.8
Diagnosis	PROM[d]	10 (30.3%)	10 (41.7%)	4 (50%)	24 (36.9%)
	PIH[e]	5 (15.2%)	1 (4.2%)	2 (25.0%)	8 (12.3%)
	Placental abruption	5 (15.2%)	2 (8.3%)	1 (12.5%)	8 (12.3%)
Delivery mode	Spontaneous labor	14 (42.4%)	9 (37.5%)	5 (62.5%)	28 (43.1%)
	Vacuum extraction	2 (6.1%)	1 (4.2%)	0 (0%)	3 (4.6%)
	Cesarean section	17 (51.5%)	14 (58.3%)	3 (37.5%)	34 (52.3%)
Maternal findings	BT[f] (℃)	36.8 ± 0.6 *	37.1 ± 0.7 *	36.7 ± 0.3	36.9 ± 0.6
	WBC[g] (/mm3)	9,150 ± 2,620 (n=21)	10,980 ± 3,570 (n=17)	10,930 ± 6,520 (n=6)	10,100 ± 3,700 (n=44)
	CRP[h] (g/dL)	1.76 ± 4.17 (n=20)	2.07 ± 3.7 (n=17)	2.13 ± 2.95 (n=6)	1.93 ± 3.76 (n=43)
Neonatal findings	UA[i] pH	7.27 ± 0.09 (n=28)	7.27 ± 0.09 (n=22)	7.28 ± 0.08 (n=8)	7.27 ± 0.09 (n=58)
	APS[j] 1min≥7	5 (15.1%)	5 (20.8%)	0 (0%)	10 (15.4%)
	APS[j] 5min≥7	1 (3.0%)	0 (0%)	0 (0%)	1 (1.5%)

* , $p<0.05$ analyzed by student t-test

NOTE: [a]CAM stage 1 means intervillositis
[b]CAM stage 2 means chorionitis
[c]CAM stage 3 means chorioamnionitis
[d]PROM means preterm rupture of membrane
[e]PIH means pregnancy-induced hypertension
[f]BT means body temperature
[g]WBC means white blood cell
[h]CRP means C-reactive protein
[i]UA means umbilical artery
[j]APS means Apgar score

Except maternal body temperature, the characteristics showed no significant difference in the three groups. Maternal body temperature showed a significant difference between stages 1 and 2 ($p<0.05$).

Table 2 shows the relationship between histological CAM and FHR patterns. The rate of tachycardia according to the severity of CAM was as follows: 3.0% (1 of 33 cases) for stage 1, 12.5% (3 of 24 cases) for stage 2, and 37.5% (3 of 8 cases) for stage 3. The number of cases with tachycardia increased with the severity of histological CAM, but the increase was not statistically significant. Baseline variability and decelerations were not associated with the severity of histological CAM.

The number of cases in which maternal fever exceeded 38.0℃ was 1 in stage 1, 2 in stage 2, and 0 in stage 3. The CRP values in all three cases were greater than 5 mg/dL. The WBC counts were less than 15,000/mm^2 and the UApH value were greater than 7.1 in these 3 cases. Of 3 cases with maternal fever greater than 38.0℃, 1 case with CAM stage 2 exhibited tachycardia and loss of variability. The other 2 cases showed no abnormal FHR patterns.

Of the 8 cases with placental abruption, 3 cases showed an abnormal FHR pattern. All 3 cases with an abnormal FHR pattern also had CAM stage 1. Deceleration was present in all 3 cases. Abnormal FHR variability was seen in 2 of the 3 cases, and tachycardia and bradycardia was seen in 1 case each. In cases of histological CAM, there was no correlation between placental abruption and an abnormal FHR pattern.

Discussion

The present study suggests that the FHR pattern is not a reliable index for diagnosing histological

Table 2 Correlation between Cardiotocogram findings and grade of Chorioamnionitis

		CAM stage 1[a] (n=33)	CAM stage 2[b] (n=24)	CAM stage 3[c] (n=8)	Total (n=65)
Baseline	Bradycardia	1 (3.0%)	0 (0%)	0 (0%)	1 (1.5%)
	Normocardia	31 (93.9%)	21 (87.5%)	5 (62.5%)	57 (87.7%)
	Tachycardia	1 (3.0%)	3 (12.5%)	3 (37.5%)	7 (10.8%)
Variability	Normal	30 (90.9%)	22 (91.7%)	8 (100%)	60 (92.3%)
	Abnormal	3 (9.1%)	2 (8.3%)	0 (0%)	5 (7.7%)
Deceleration	Negative	21 (63.6%)	17 (70.8%)	6 (75.0%)	44 (67.7%)
	Positive	12 (36.4%)	7 (29.2%)	2 (25.0%)	21 (32.3%)

N.S.: analyzed by student t-test

NOTE: [a]CAM stage 1 means intervillositis
[b]CAM stage 2 means chorionitis
[c]CAM stage 3 means chorioamnionitis

CAM, because the FHR pattern was normal in most cases of histological CAM. Although some investigators have shown an association between clinical CAM and abnormal FHR patterns, such as tachycardia[5,6], reduced variability[6–8], and decelerations[8,9], these results are ambiguous. Carroll et al.[6] have reported that a lower biophysical profile score, including increased baseline and reduced FHR variability, was associated with intrauterine infection in cases of preterm premature rupture of membranes; however, the results of these tests were normal in the majority of pregnancies with positive results of cultures of amniotic fluid or fetal blood. Del Valle et al.[10] have suggested that an abnormal FHR pattern is not useful for predicting perinatal infection (CAM, neonatal sepsis, and neonatal pneumonia) because of its low sensitivity (46%; specificity was 95%).

In the present study, only 3 of 65 cases of histological CAM (4.6%) were associated with a maternal fever greater than 38.0℃. Smulian et al.[14] have reported that clinical CAM is not supported by histologic evidence of infection in 38.1% of cases. These findings indicate that the pathophysiology of histological CAM is not the same as that of clinical CAM. Salafia et al.[15] have suggested that some cases of histologic inflammation could be due to a variety of noninfectious causes, including fetal hypoxia, amniotic fluid pH changes, immunologic responses to fetal tissues, meconium, and other nonspecific reactive responses. We believe that the diverse causes of histological CAM are responsible for the variety of FHR patterns.

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