CASE REPORT

Maternal bradycardia occurring prior to onset of HELLP syndrome in a woman with pre-eclampsia

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SUMMARY

A 36-year-old nulliparous woman developed pre-eclampsia at gestational week (GW) 28^{-6/7}. Cardiac status was checked regularly. Heart rate of 93 beats per minute (bpm) with left atrial diameter (LAD) of 35 mm, left ventricular hypertrophy and inferior vena cava diameter (IVCD) of 8 mm at GW 32^{-0/7} decreased to 48 bpm with an expanded IVCD to 25 mm, dilated left atrium (LAD to 39 mm), increased pulmonary arterial pressure, increased systemic vascular resistance (approximate 3000 dyn s/cm⁵) and biphasic intrarenal venous flow pattern 3.5 hours prior to childbirth at GW 32^{-3/7}. Epigastralgia, tachycardia (160 bpm) and marked hypertension (201/111 mm Hg) occurring 2 hours after echocardiography necessitated caesarean section, with subsequent development of HELLP syndrome. Acute fluid shift from the splanchnic vasculature to central vasculature may have occurred causing HELLP syndrome as a result from vasospasm associated with sympathetic hyperactivity. The cause of bradycardia prior to tachycardia remains unclear.

BACKGROUND

Maternal heart rate (HR) increases gradually during pregnancy.¹ Pre-eclampsia is a state of sympathetic overactivity,² and sympathetic hyperactivity usually causes tachycardia in non-pregnant subjects.³ However, maternal HR is actually lower in women with pre-eclampsia than in healthy pregnant women; third trimester HR is significantly lower for women with pre-eclampsia than that in healthy control women (71±14 vs 85±10 beats per min (bpm), respectively).¹

We have focused on cardiac changes on echocardiography in pregnant women, especially in women with pre-eclampsia and/or twin pregnancies, because pre-eclampsia and twin pregnancies are prominent and consistent risk factors for peripartum cardiomyopathy.⁴⁻⁷ Here, we report a woman with pre-eclampsia in whom marked maternal bradycardia occurred prior to acute increases in blood pressure (BP) and HR and the onset of HELLP syndrome. This presentation was conducted with informed consent from the patient.

CASE PRESENTATION

A 36-year-old nulliparous Japanese woman developed hypertension (142/94 mm Hg) and significant proteinuria (spot urine protein:creatinine ratio (mg/mg) of 0.33) at gestational week (GW) 27^{-6/7} and 28^{-6/7}, respectively, and was diagnosed with

pre-eclampsia. The patient was hospitalised at GW 30^{-0/7} with BP of 135/95 mm Hg while receiving no medication (table 1). Haemoconcentration (haemoglobin concentration, 14.0 g/dL; haematocrit value (Ht), 41.6%), normal platelet count and blood chemistry were seen on admission (table 1). BP remained stable below 140/100 mm Hg without medication until GW 31^{-6/7} at which time nifedipine was required temporarily to stabilise BP. Echocardiography on GW 32^{-0/7} showed HR of 93 bpm, slightly enlarged left atrium (left atrial diameter (LAD) from parasternal long-axis view of 35 mm), left ventricular (LV) hypertrophy (LVH, LV mass index corrected by prepregnancy body surface area (LVMI) of 107 g/m²), normal LV ejection fraction (LVEF, 67%) and inferior vena cava diameter (IVCD) of 8 mm (table 1, figure 1A, video 1). In the morning (06:00) of the day of delivery at GW 32^{-3/7}, HR of 60 bpm with BP of 153/94 mm Hg were noted (figure 1A) in this patient. Because of her dyspnoea, echocardiography performed 1.6 hours later at 07:40 demonstrated a further reduction in HR to 48 bpm (video 1) and pulse pressure (BP to 117/97 mm Hg), dilated left atrium (LAD of 39 mm), markedly increased IVCD (to 25 mm) and pulmonary arterial pressure of 36/14 mm Hg for pulmonary arterial systolic/diastolic pressure and biphasic intrarenal venous flow pattern (figure 1B). Cardiac output was decreased to 2.39 L/min resulting in a calculated high systemic vascular resistance of approximate 3000 dyn s/cm⁵ at that time. Two hours after echocardiography, epigastric pain, tachycardia (160 bpm) and marked hypertension (201/111 mm Hg) (figure 1A) occurred and necessitated emergency caesarean section at 11:18, giving birth to a male infant weighing 1124 g with Apgar scores of 8 (1 min) and 9 (5 min) and umbilical cord arterial blood pH of 7.30 in this patient. The patient was shown to have HELLP syndrome on the morning after childbirth (table 1, figure 1A).

INVESTIGATIONS

Plasma B-type natriuretic peptide level determined immediately before caesarean section was markedly elevated (table 1). Detailed analysis on echocardiography (video 1) performed immediately before caesarean section revealed several findings. Cardiac index was markedly reduced to 1.36 L/min/m² with a reduced HR of 48 bpm. Shortening fraction, average of systolic septal and lateral mitral annular velocities (s') and average of early diastolic septal and lateral mitral annular velocities (e') were 31%, 10.5 cm/s and 12.9 cm/s, respectively (table 1). Thus, there was

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Table 1 Perinatal changes in physical findings, blood variables and cardiac parameters

	Gestational week		32 ^{-3/7} * (time)			Postpartum day (PPD)		
	30 ^{-0/7}	32 ^{-0/7}	(06:00)	(07:40)	(11:00)	1	5	7
Body weight (kg)	67.1	68.4	71.0	NA	NA	NA	63.9	62.8
Platelet ($\times 10^9/L$)	230	173	179	NA	NA	94	136	233
AST (IU/L)	15	18	40	NA	NA	162	NA	22
LDH (IU/L)	176	222	175	NA	NA	465	234	224
BNP (pg/mL)	NA	NA	NA	211	NA	NA	NA	NA
Blood pressure (mm Hg)	135/95	127/83	153/94	117/97	201/111	135/97	135/94	133/95
Heart rate (bpm)	82	93	60	48	160	107	90	96
LVDd (mm)	NA	43	NA	45	NA	NA	44	NA
LAD (mm)	NA	35	NA	39	NA	NA	34	NA
LVMpl (g/m ²)	NA	107	NA	115	NA	NA	91	NA
IVCD (mm)	NA	8	NA	25	NA	10	12	NA
Shortening fraction (%)	NA	37	NA	31	NA	NA	36	NA
LVEF (%)	NA	67	NA	59	NA	NA	67	NA
E/A	NA	0.71	NA	2.22	NA	NA	NA	NA
S/D	NA	1.71	NA	NA	NA	NA	NA	NA
E/e'	NA	6.8	NA	6.1	NA	NA	NA	NA
s' (cm/s)	NA	11.7	NA	10.5	NA	NA	NA	NA
e' (cm/s)	NA	8.5	NA	12.9	NA	NA	NA	NA
PAP (mm Hg)	NA	NA/9	NA	36/14	NA	NA	24/9	NA

*On the day of delivery.

AST, aspartate aminotransferase; bpm, beats per minute; BNP, B-type natriuretic peptide; e', average of early diastolic septal and lateral mitral annular velocities; LDH, lactate dehydrogenase; LAD, left atrial diameter; LVDd, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVMpl, left ventricular mass index corrected by prepregnancy body surface area; NA, not available; PAP, e', average of early diastolic septal and lateral mitral annular velocities; E/A, ratio of early to late diastolic transmitral flow velocity; E/e', ratio of early diastolic mitral flow velocity to e'; pulmonary arterial pressure; s', average of systolic septal and lateral mitral annular velocities; S/D, systolic pulmonary venous flow velocity to antegrade diastolic pulmonary venous flow velocity ratio.

no impairment of LV systolic or diastolic functions on the day of delivery. Echocardiography performed 3 days before delivery (at GW 32^{-0/7}) suggested subnormal LV diastolic function caused by LVH showing a ratio of early to late diastolic transmitral flow velocity (E/A) of 0.71, systolic pulmonary venous flow velocity to antegrade diastolic pulmonary venous flow velocity ratio

(S/D) of 1.71, e' of 8.5 cm/s and ratio of early diastolic mitral flow velocity to e' (E/e') of 6.8 in the presence of normal LV contractility monitored by LVEF (67%) and s' (11.7 cm/s) (table 1). These findings together with a very acute increase in HR 2 hours after echocardiography suggested that myocardial damage was unlikely to have been responsible for the bradycardia in this patient.

TREATMENT

Fluid replacement (500–1500 mL extracellular fluid/day) given on and after GW 30^{-3/7} under monitoring of maternal weight, Ht and IVCD did not decrease Ht level (lowest Ht was 39.0%

Figure 1 Perinatal changes in various parameters in this patient. (A) Changes in systolic blood pressure (BP), heart rate (HR) and serum aspartate aminotransferase (AST) level. (B) Inferior vena cava diameter (IVCD) and intrarenal artery and vein flow patterns immediately before caesarean section at GW 32^{-3/7} (middle panel) and on postpartum day (PPD) 5 (bottom panel). It is interesting to note the gradual decrease in HR, markedly dilated IVCD and biphasic intrarenal vein flow pattern (middle panel) prior to the acute increase in BP and HR and the manifestation of HELLP syndrome.

Video 1 Echocardiography recorded at gestational week (GW) 32^{-0/7} and at 07:40–08:00 on the day of caesarean section (GW 32^{-3/7}) in this patient.

at GW 31^{-6/7} after fluid replacement) with a modestly enhanced body weight gain (weight gain of 3.9 kg during the last 2 weeks of pregnancy). Continuous intravenous nicardipine (24 mg/day) was given for 2 days (GW 31^{-6/7} and GW 32^{-0/7}) to maintain BP below 160/100 mm Hg. Intramuscular betamethasone (12 mg) was given twice at GW 32^{-0/7} and GW 32^{-1/7} to facilitate fetal lung maturation. Intravenous 1 mg nicardipine was given twice immediately after severe hypertension onset followed by a continuous nicardipine infusion (1 mg/hour) for 24 hours. Continuous intravenous magnesium sulfate (1.0 g/hour) was given for 24 hours (starting immediately before caesarean section) to reduce the risk of eclamptic fit. Oral nifedipine (20 mg/day) was given for 30 days until postpartum day (PPD) 30.

OUTCOME AND FOLLOW-UP

The presumably increased central venous pressure (CVP) suggested by increased LAD and IVCD before caesarean delivery decreased with decreases in LAD (table 1) and IVCD (figure 1B), and both LVH (monitored by LVMpI) and pulmonary hypertension improved on PPD 5 (table 1). Spot urine protein:creatinine ratio of 0.38 and normalised platelet count and serum AST/LDH levels were seen on PPD 7. The patient left hospital on PPD 8 with BP of 133/95 mm Hg on treatment with 20 mg nifedipine daily with a body weight of 62.8 kg. The BP was 133/83 mm Hg without medication, urine protein was negative on dipstick test and body weight was 62.7 kg on PPD 35 in this patient. The child with hypospadias left hospital at age 99 days with body weight of 3710 g.

DISCUSSION

This patient with pre-eclampsia exhibited bradycardia (HR of 48 bpm) prior to the acute increase in HR and BP and onset of HELLP syndrome mimicking paroxysmal sympathetic hyperactivity.³ Marked increases in IVCD, LAD and biphasic intrarenal vein flow pattern were seen at the time of marked bradycardia, suggesting the occurrence of increased CVP and preload. The biphasic intrarenal vein flow pattern is likely to occur in patients with increased CVP.⁸ These indicated that increase in the central fluid volume occurred in this patient.

Mechanisms that led to severe bradycardia prior to tachycardia were unknown. However, this patient had epigastric pain, tachycardia (160 bpm) and marked hypertension (201/111 mm Hg) 2 hours after echocardiography and developed HELLP syndrome. Vasospasms have been reported in the middle and posterior cerebral and hepatic arteries in cases of severe pre-eclampsia and HELLP syndrome with peripheral ischaemic changes.⁹ Sympathetic overactivity is a characteristic feature in women with pre-eclampsia² and may have occurred resulting in tachycardia and marked hypertension in this patient. Splanchnic organs constitute 10% of the body weight, but contain 25% of the total blood volume, and thus the splanchnic vasculature serves as an important blood reservoir for the circulatory system.^{10 11} Sympathetic activation expels blood from splanchnic capacitance vessels, producing a rapid increase in venous return up to 800 mL.^{10 11} Resulting inadequate perfusion to splanchnic organs may have caused epigastric pain and liver dysfunction in this patient. To our knowledge, this is the first case in which bradycardia and tachycardia were documented in a short time in a woman with pre-eclampsia. This case may represent dysregulation of balance in sympathetic and parasympathetic functions showing unexplained bradycardia with increased central fluid volume.

The circulating plasma volume is reduced by approximately 20% in women with pre-eclampsia,¹² as suggested in this patient

with haemoconcentration, as evidenced by Ht of 41.6% on admission; the frequency of Ht >41% is rare, occurring in <1.0% of women immediately before birth.¹³ Fluid replacement given in this patient was ineffective for amelioration of haemoconcentration, but may have caused expansion of interstitial fluid volume, as suggested by greater maternal weight gain of 3.9 kg in the last 2 weeks of pregnancy (median (2.5th–97.5th) weight gain in the last 2 weeks of pregnancy is 0.76 (–1.66–4.01) kg for otherwise healthy Japanese women¹⁴). However, fluid replacement is known to be effective for lowering BP in patients with pre-eclampsia.¹⁵ It remains unclear whether fluid replacement was beneficial in this patient.

Learning points

- ▶ Tachycardia following bradycardia was documented in a pre-eclampsia woman with HELLP syndrome.
- ▶ Greater inferior vena cava diameter, left atrial diameter and biphasic intrarenal vein flow pattern indicated increase in the central fluid volume in this patient.
- ▶ Sympathetic overactivity may have expelled the blood reserved in the splanchnic organs causing increased central fluid volume in this patient.
- ▶ This case may represent dysregulation of balance in sympathetic and parasympathetic functions with unexplained bradycardia prior to sympathetic hyperactivity.

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