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Unusual clinical course of preeclampsia heralded by generalized edema

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Running foot: Unusual preeclampsia heralded by edema

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Abstract

Background: Preeclampsia monitored by the amount of proteinuria usually does not show amelioration during pregnancy.

Case: A 37-year-old nulliparous woman was admitted to our hospital at gestational week (GW) $24^{-1/7}$ due to rapid weight gain (6.2 kg/4 weeks) and oligohydramnios. Hypertension (151/91 mmHg) appeared at GW $25^{-0/7}$ and proteinuria not detected at GW $24^{-0/7}$, became significant (0.55 g/day) at GW $25^{-2/7}$. During the two successive weeks after administration of betamethasone at 12 mg twice and transabdominal amnioinfusion with 250 mL of Ringer's acetate solution at GW $25^{-3/7}$, generalized edema, proteinuria, and thrombocytopenia markedly improved: body weight, 78.0 – 69.0 kg; proteinuria (g/day), 7.1 – 1.3; and platelet count ($\times 10^9$/L), 111 – 230. However, intrauterine infection accompanied by non-reassuring fetal status necessitated emergency cesarean section at GW $28^{-3/7}$.

Conclusion: Extrordinary body weight gain can herald the occurrence of preeclampsia and this weight gain together with signs of preeclampsia can ameliorate even during pregnancy, although its mechanism is unclear.

Keywords: gestational edema, preeclampsia, thrombocytopenia, vascular permeability

Introduction

Women with preeclampsia are likely to show excessive water retention [1]. Although generalized edema can precede the development of preeclampsia [2], there is as yet no technical term applicable to the condition of edema alone. Preeclampsia usually does not show amelioration during pregnancy. **Here, we present a pregnant woman in whom preeclampsia was heralded by generalized edema and clinical signs of preeclampsia acutely ameliorated during pregnancy.**

Presentation of the case

This study was approved by the institutional review board of the Hokkaido University Hospital and was undertaken following the provisions of the Declaration of Helsinki.

A 37-year-old nulliparous Japanese woman presented with marked edema (weight gain of 6.2 kg/4 weeks) (Fig. 1) and oligohydramnios (amniotic fluid index [AFI] of 4.8 cm) in the absence of hypertension, proteinuria, or placental edema and was admitted to our hospital at gestational week (GW) $24^{-1/7}$. Hypertension (151/91 mmHg) and proteinuria (0.55 g/day) appeared at GW $25^{-0/7}$ and GW $25^{-2/7}$, respectively. **Primary aldosteronism**, autoimmune diseases, or thyroid diseases were considered unlikely by endocrinologists and immunologists (Table 1). Administration of betamethasone for fetal lung maturation (intramuscular 12 mg twice) and amnioinfusion with 250 mL of Ringer's acetate solution for oligohydramnios (AFI of 0.4 cm) were performed at GW $25^{-3/7}$ (Fig. 1). An AFI of 11.5 cm at GW $25^{-4/7}$ gradually decreased to 3.8 cm at GW $27^{-6/7}$. Treatment with oral nifedipine (20 mg/day) was initiated at GW $26^{-0/7}$. The maternal body weight began to decrease after showing a peak value at GW $25^{-5/7}$ and platelet counts began to increase after showing a nadir value at GW $26^{-6/7}$, while

hematocrit values were stable (Fig. 1). Proteinuria (g/day) also began to decrease after showing a peak value of 7.1 at GW $26^{-6/7}$ to 1.3 at GW $27^{-3/7}$, respectively, while blood pressure remained high (140 – 170/75 – 95 mmHg).

Four days after the second amnioinfusion (250 mL of Ringer's acetate solution) at GW $27^{-6/7}$ for oligohydramnios (AFI of 3.8 cm), the patient exhibited fever of 38.6℃ with elevated C-reactive protein level (5.7 mg/dL) and WBC count (20200/μL), as well as non-reassuring fetal status at GW $28^{-3/7}$. A growth restricted (-1.45 SD) female infant weighing 820 g was born by emergency cesarean section. Pathological examination of the placenta revealed chorioamnionitis (stage III). The infant survived septicemia with *Abiotrophia defectiva* and left our hospital on hospital day 85. Magnetic resonance imaging (MRI) of the infant's brain performed on hospital day 82 was unremarkable. The mother leaving our hospital on postpartum day 8 showed normal blood pressure (127/69 mmHg) and non-significant proteinuria (negative on dip stick test) at 1 month postpartum.

Discussion

This patient exhibited two unusual features of pregnancy. First, her preeclampsia was heralded by extraordinary weight gain between GW 20 and 24. Second, her preeclampsia monitored by changes in body weight (degree of edema), proteinuria, and platelet counts showed amelioration during pregnancy.

We previously encountered a woman who exhibited rapid weight gain (6.0 kg in the last 7 days of pregnancy) with gradual declines in antithrombin activity and platelet count until delivery [2]. In this previous case, the risk of pulmonary edema necessitated cesarean section at GW 37 in the absence of hypertension and proteinuria, and

pulmonary edema actually developed postpartum followed by hypertension, but the diagnosis of preeclampsia had to wait until 5 days after delivery at which time proteinuria developed [2]. Thus, a type of preeclampsia with edema as its initial sign indeed exists. The present case also showed a gradual decline in platelet count (Fig. 1) and modestly reduced antithrombin activity (72% of normal activity level). Pregnant women with reduced antithrombin activity and/or platelet counts are suggested to be suffering from increased blood vessel permeability [3, 4]. The appearance of edema is likely a consequence of endothelial leakage of plasma into the interstitial space. Consequently, plasma volume is reduced by approximately 20% in women with preeclampsia [5] and more in women with eclampsia [6]. The rapid and extraordinary weight gain in our patient may be explained by the same mechanism as that in women with preeclampsia.

Amounts of protein in the urine increase with advancing gestation irrespective of the presence or absence of hypertension [7]. In the presence of increased blood vessel permeability, adequate water intake results in edema formation with stable hematocrit value, but insufficient water intake results in increased hematocrit value, and finally a decrease in body weight designated as “dehydration.” Thus, in the presence of increased blood vessel permeability, maternal body weight is unlikely to decrease in the absence of changes in hematocrit value. However, the present case exhibited marked weight reduction with stable hematocrit value and a decrease in proteinuria. As the period until delivery after the diagnosis of preeclampsia is approximately 2 weeks [7], this patient received steroid administration and amnioinfusion, resulting in an increase of AFI from 0.4 to 11.5 cm. It remains unclear whether these treatments contributed to the favorable

111 changes in various parameters seen in this patient.

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113 **Disclosure**

114 All authors declare that they have no financial relationship with a biotechnology

115 manufacturer, a pharmaceutical company, or other commercial entity that has an interest

116 in the subject matter or materials discussed in the manuscript.

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Figure Legend

Figure 1: Changes in maternal body weight (○), platelet counts (●), and hematocrit value (×)

PPD, postpartum day

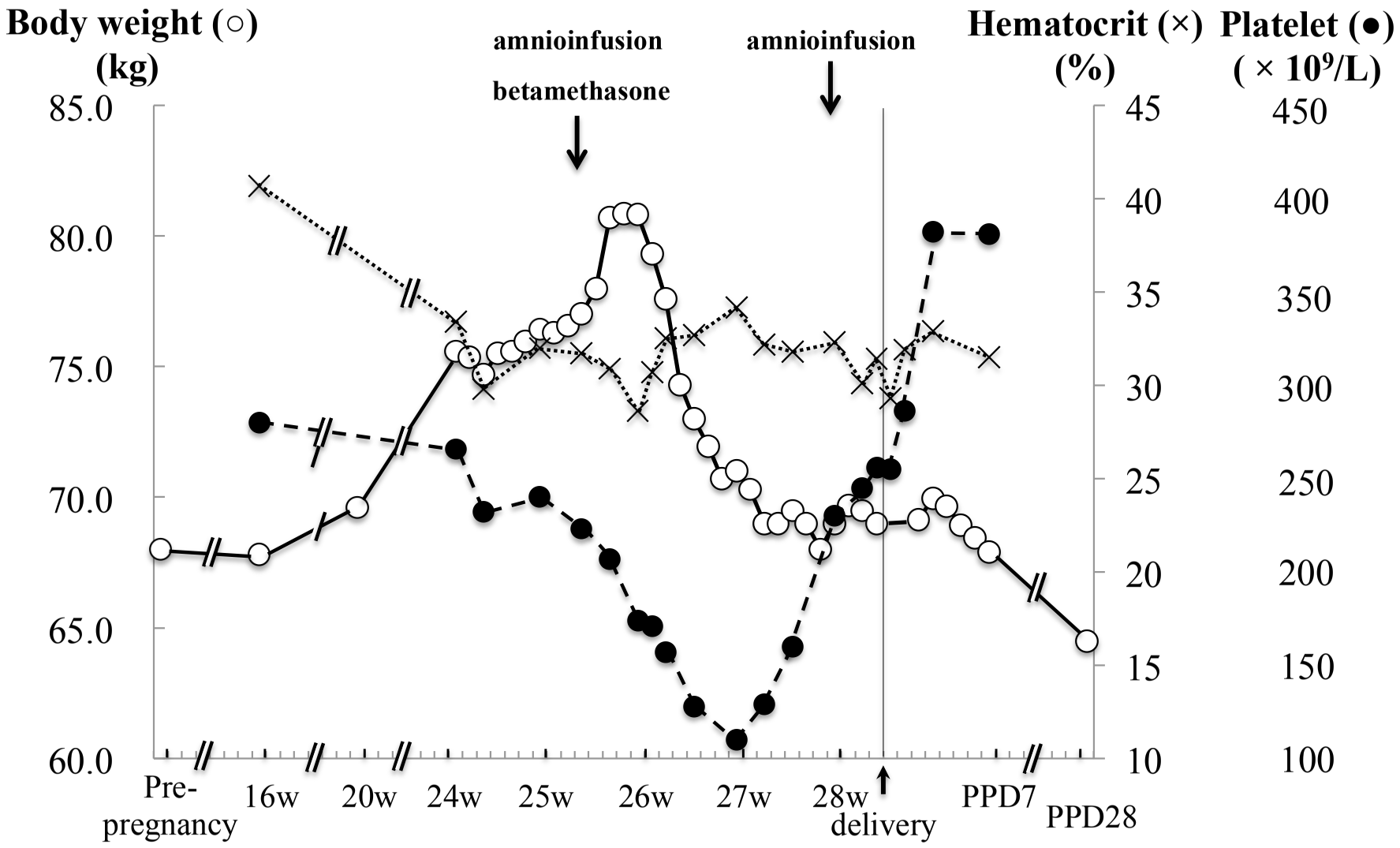
Body weight (○)
(kg)
85.0
80.0
75.0
70.0
65.0
60.0
amnioinfusion
betamethasone
amnioinfusion
Hematocrit (×)
(%)
45
40
35
30
25
20
15
10
Platelet (●)
(× 10⁹/L)
450
400
350
300
250
200
150
100
Pre-
pregnancy
16w
20w
24w
25w
26w
27w
28w
delivery
PPD7
PPD28

Table 1. Results of laboratory work-up and Doppler study

Antithrombin activity [% of normal activity level]; 78 ($24^{-0/7}$), 72 ($25^{-2/7}$), 86 ($27^{-6/7}$)

AST [IU/L]; 12 ($24^{-0/7}$), 13 ($28^{-3/7}$), 16 (PPD 3); LDH (IU/L), 161 ($24^{-0/7}$), 137 ($28^{-3/7}$), 190 (PPD 3)

PAC [ng/L]; 124 ($24^{-6/7}$), 115 ($26^{-0/7}$): PRA [ng/mL/hour]; 2.8 ($24^{-6/7}$), 2.7 ($26^{-0/7}$)

TSH; 2.16 μIU/mL ($24^{-6/7}$): Free T4; 1.1 ng/dL ($24^{-6/7}$)

NT-proBNP [ng/L]; 992 ($26^{-0/7}$), 79 ($27^{-6/7}$)

IgA; 147 mg/dL ($24^{-2/7}$): IgG; 735 mg/dL ($24^{-2/7}$): IgM; 186 mg/dL ($24^{-2/7}$):

IgE; 107 mg/dL ($24^{-2/7}$)

C3 *; 95 mg/dL ($24^{-2/7}$): C4*; 7 mg/dL ($24^{-2/7}$): CH50*; 31 U/mL ($24^{-2/7}$)

Rheumatoid factor; 0.9 IU/mL ($24^{-2/7}$): Antinuclear antibody; negative ($24^{-2/7}$)

Anti-cardiolipin antibody; ND ($25^{-2/7}$): Lupus anticoagulant; ND ($25^{-2/7}$)

Anticardiolipin-β2 glycoprotein I complex antibody; ND ($26^{-1/7}$)

Umbilical artery pulsatility index; 1.52 ($25^{-2/7}$), 0.99 ($28^{-2/7}$)

Umbilical artery resistance index; 0.76 ($25^{-2/7}$), 0.65 ($28^{-2/7}$)

Fetal middle cerebral artery pulsatility index; 1.27 ($25^{-2/7}$), 1.30 ($28^{-2/7}$)

Fetal middle cerebral artery resistance index; 0.73 ($25^{-2/7}$), 0.74 ($28^{-2/7}$)

Gestational week at examination is indicated in parenthesis.

PPD 3, postpartum day 3; AST, Aspartate aminotransferase; LDH, Lactate dehydrogenase;

PAC, plasma aldosterone concentration; PRA, plasma renin activity; TSH, thyroid stimulating hormone;

NT-proBNP, N-terminal fragment of precursor protein brain-type natriuretic peptide;

Ig, Immunoglobulin; *, Complement; ND, not detected