DOI：10.6314/JIMT.202206_33(3).07 內科學誌 2022：33：233-240

Sustained Preeclampsia into the Postpartum Period Complicated with Severe Pericardial Effusion: A Case Report

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Abstract

In the natural course of preeclampsia, proteinuria usually begins to improve within a few days after delivery. In heavy proteinuria, complete resolution may take weeks to months. In this case, hypertension and proteinuria persisted for 3 months after delivery. In addition, an uncommon complication—pericardial effusion—also occurred. This 34-year-old woman delivered a baby two months ago, and she had type 2 diabetes mellitus for two years. During the second trimester, heavy proteinuria with hypertension was noted; therefore, preeclampsia was diagnosed. However, tachycardia with four-limbs edema persisted after delivery, and a large amount of pericardial effusion was detected by transthoracic echocardiography. The renal biopsy revealed diabetic nephropathy superimposed with glomerular injury of preeclampsia. Preeclampsia may be complicated by severe pericardial effusion and fluid overload, and its symptoms may persist after delivery. Glycemic and intensive blood pressure control could improve the urine protein/creatinine ratio. (J Intern Med Taiwan 2022; 33: 233-240)

Key Words: Preeclampsia, Postpartum, Pericardial effusion

Introduction

In the natural course of preeclampsia, proteinuria usually begins to improve within a few days after delivery. In women with heavy proteinuria, complete resolution may take weeks to months[1]. However, in this report, we describe a case of hypertension and proteinuria persisting for 3 months after delivery. In addition, an uncommon complication—pericardial effusion—occurred.

Case report

Before admission, the patient had just successfully delivered a baby (Gravida: 1 Para: 1 Spontaneous abortion: 0 Artificial abortion: 0) two months ago. She had a history of type 2 diabetes mellitus (HbA1c: 5.7%) for two years with regular medical control (glimepiride) before pregnancy. She had severe non-proliferative diabetic retinopathy by ophthalmoscope exam initially. During the second trimester, hypertension (179/92mmHg), heavy pro-

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teinuria (3+), hematuria (erythrocytes 1-4 per high-power field) were documented and she also had anemia (hemoglobin 10.4 g/dl). However, platelet count and liver function were all within normal limit. (platelet count 321,000/μl; alanine aminotransferase 20 U/liter). Thus, preeclampsia was impressed. However, hypertension and general edema were still presented one month after delivering the baby. Therefore, losartan/hydrochlorothiazide, labetalol and furosemide were prescribed but in vain. She had progression of the dyspnea, but she did not have fever, chills, abdominal pain, or dysuria.

On examination, the patient was alert and fully oriented. Her body mass index (the weight in kilograms divided by the square of the height in meters) was 30.6. Her temperature was 37°C, her blood pressure was 197/115 mmHg, her pulse was 110 beats per minute, her respiratory rate was 20 breaths per minute, and her oxygen saturation was 95% while the patient was breathing with supplemental oxygen (2 liters per minute through a nasal cannula). There were coarse crackles over her bilateral lower lung fields. Her heart sound was regular without any murmur. Four limbs with pitting edema (++) was noted. The other findings of the physical examination were unremarkable.

Her fasting blood glucose level was 178 mg per deciliter (9.9 mmol per liter). An electrocardiogram showed sinus tachycardia but otherwise normal. Her laboratory test results and urine analysis are shown in Table 1. A chest radiograph (Figure 1a) was performed and showed bilateral pleural effu-

Table 1. Laboratory data and urine analysis

Variable	Reference Range	On Admission	Hospital Day 33
Blood			
Hemoglobin (g/dl)	11.6–14.8	8.7	8.2
Hematocrit (%)	34.0–44.0	28.3	25.6
Platelet count (per μl)	150,000–400,000	298000	249000
White-cell count (per μl)	3200–9200	4500	8100
Differential count (%)			
Neutrophils	45-70	59.3	60.7
Lymphocytes	20-45	30.8	31.1
Monocytes	2-8	8.6	6.1
Eosinophils	0-4	0.9	1.9
Basophils	0-1	0.4	0.2
Plasma cells (%)	0	0	
Prothrombin time (sec)	9.4-12.5	10.9	11.1
Prothrombin-time international normalized ratio (sec)	0.9-1.1	1.05	0.95
Activated partial-thromboplastin time (sec)	26.0-38.0	29.4	26.9
N-terminal pro–B-type natriuretic peptide (pg/ml)	0-900	> 25000	
Sodium (mmol/liter)	136–145	132	140.6
Potassium (mmol/liter)	3.5–5.0	4.5	3.80
Urea nitrogen (mg/dl)	6-20	41	46
Creatinine (mg/dl)	0.57-1.11	1.77	1.12
Glucose (mg/dl)	70-100	178	
Magnesium (mg/dl)	1.9-2.5		2.1

Table 1. Laboratory data and urine analysis (Continued)

Variable	Reference Range	On Admission	Hospital Day 33
Alanine aminotransferase (U/liter)	2-40	15	11
Aspartate aminotransferase (U/liter)	5-34	32	13
Albumin (g/dl)	3.5-5.2	1.8	2.9
C-reactive protein (mg/liter)	<5	19	
Arterial blood gas			
Fraction of inspired oxygen			
pH	7.35-7.45	7.432	
Partial pressure of carbon dioxide (mm Hg)	32-42	30.6	
Partial pressure of oxygen (mm Hg)	75-100	73.1	
Urine			
Color	Amber	Yellow	Yellow
Specific gravity	1.005–1.030	1.016	1.018
Glucose	Negative	1+	Negative
pH	5.0–8.0	6.0	7.5
Nitrite	Negative	Negative	Negative
Blood	Negative	2+	2+
Erythrocytes (per high-power field)	0–5	20-29	30-49
Leukocytes (per high-power field)	0-5	5-9	5-9
Protein	Negative	3+	3+
Urine total protein: creatinine ratio (mg/g)	<150	8634.8	14873.8

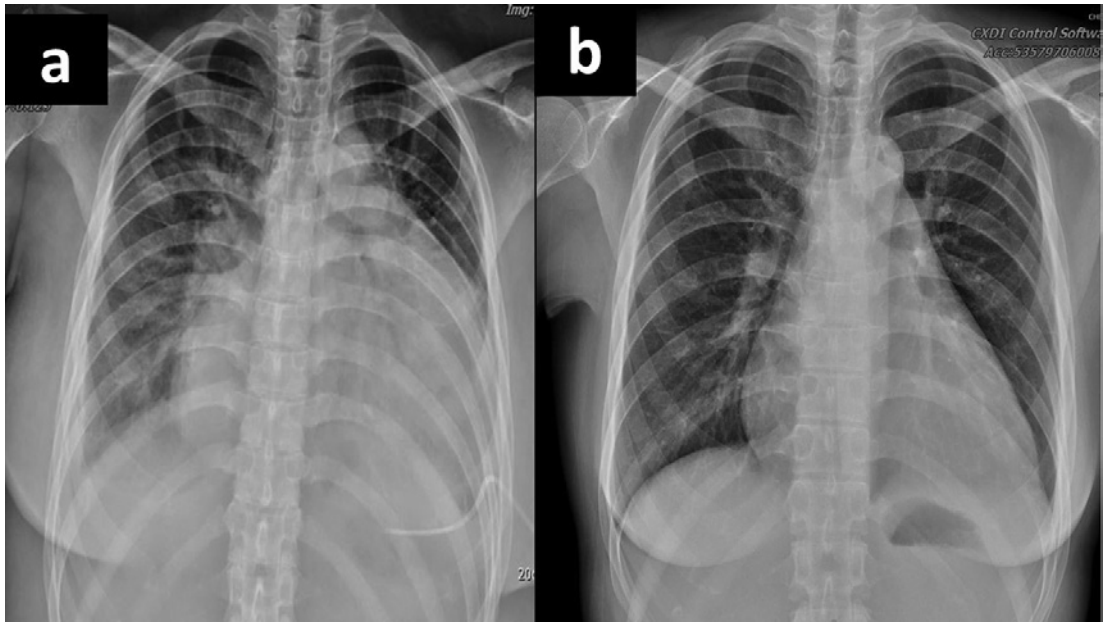

Figure 1. Chest radiograph from hospitalization to discharge. (a) pericardial effusion status post pericardiocentesis and pigtail insertion. (b) follow up at outpatient clinic after discharge in two months.

sion with cardiomegaly. A transthoracic echocardiogram revealed a large amount of pericardial effusion without tamponade signs (Figure 2), as well as adequate global left ventricle performance. There was no chamber dilation or regional wall motion abnormality.

We undertook a differential diagnosis of this patient. In this case, the cause of her pericardial effusion was not apparent. Confirming the precise etiology generally requires sampling of the effusion for laboratory analysis[2] (Table 2). Thus, thoracentesis and pericardiocentesis were performed for symptom relief and further surveys. Pericardial fluid and pleural fluid analysis showed clear appearance with yellow color. Transudate was impressed due to normal range of protein, lactate dehydrogenase and glucose. Cytology revealed no malignant cells. Her chest radiograph was followed up (Figure 1b). The average amount of pericardial drainage was 372 milliliters/day for 14 days.

So far, the clues are massive pericardial effusion and nephrotic range proteinuria. To make our thinking process more clearly, we list the possible causes of pericardial effusion and proteinuria separately in Table 3 and consider possible diseases when they occur together.

The differential diagnoses of pericardial effusion included pericarditis, infective endocarditis and tuberculosis infection. However, this patient had no symptoms of inflammation or any other infection signs, such as fever or leukocytosis, which made infection an unlikely diagnosis. Pericardial fluid analysis showed transudate, and a culture revealed negative findings.

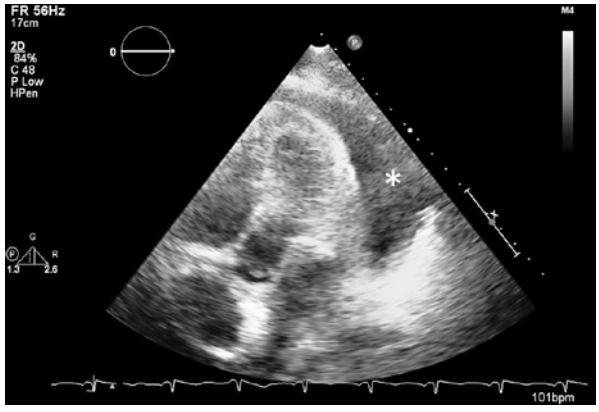

Figure 2. Echocardiography of pericardial effusion (∗).

Table 2. Pericardial fluid and pleural fluid analysis

Variable	Pericardial fluid	Pleural fluid
Appearance	clear	clear
Color	yellow	yellow
Total Protein [g/dL]	1.3	1.0
LDH [IU/L]	70	90
Glucose[mg/dL]	455	168
PH	7.94	
RBC[/uL]	606	300
Total Nucleated Cell [/uL]	14	185
Lymphocyte	4	139
Neutrophil	10	24
Mesothelial cell	0	9
Histocyte	0	13
Aerobic culture	No growth	No growth
Tuberculosis culture	No growth	No growth
Gram stain	Not found	Not found
Acid-fast stain	Negative	Negative
Cytology exam	No malignant cells were found	No malignant cells were found

Table 3. Common etiology of pericardial effusion and nephrotic syndrome

Pericardial effusion	Nephrotic syndrome
Acute pericarditis	Minimal change disease
Post myocardial infarction or cardiac surgery	Focal segmental glomerulosclerosis
Malignancy	Membranous nephropathy
Rheumatologic disorder	Diabetes mellitus
Renal failure (acute or chronic)	Amyloidosis
Trauma	Rheumatologic disorder
Mediastinal radiation	

Heart disease-related pericardial effusion was possible. This patient had symptoms of dyspnea and exercise intolerance, but there was no orthopnea or jugular vein engorgement. She did not have a history of congestive heart failure, myocardial infarction or any cardiac surgery before. On physical examination, there were no signs of poor perfusion, such as cold extremities, hypotension, and mental status changes. However, laboratory data showed elevated N-terminal pro-brain natriuretic peptide (>25000 pg/ml). Thus, a transthoracic echocardiogram was arranged and revealed hyperdynamic contractility of left ventricle performance with an ejection fraction of 89.1%, but there was a large amount of pericardial effusion.

Malignancy should be considered in any case with pericardial effusion whose cause is unknown. Fortunately, the patient's pericardial fluid cytology showed no malignant cells.

In a young woman with pericardial effusion, a careful history directed toward the presence of a coexisting rheumatologic disorder such as systemic lupus erythematosus should be obtained. However, this patient did not have a butterfly rash, joint pain or other systemic lupus erythematosus signs. Moreover, she had no fatigue, muscle weakness or other hypothyroidism-associated symptoms. Laboratory data revealed a normal range of free thyroxine and thyroid-stimulating hormone.

Systemic disease should be taken into account for this patient, who had symptoms of general edema, pleural effusion and pericardial effusion. Due to heavy proteinuria, an elevated total urine protein creatinine ratio and hypoalbuminemia, nephrotic syndrome could be a possible diagnosis. To distinguish the etiology of glomerulonephritis from nephrotic syndrome, serologic studies including antinuclear antibody (ANA) tests and complement levels (complement 3/ complement 4, C3/C4) were performed. Negative ANA tests and normal C3 and C4 levels were reported. In most cases, proteinuria typically results from podocyte injury, which is a hallmark of primary nephrotic syndrome, including adult minimal change disease, focal segmental glomerulosclerosis (FSGS), and membranous nephropathy[3].

Initially, because a diagnosis of FSGS was suspected, steroid therapy with intravenous methylprednisolone 500 mg once a day was given for three days, followed by intravenous methylprednisolone 40 mg twice a day. However, her heavy proteinuria with pericardial effusion did not improve (Table 1). Afterwards, cyclosporine was used but it was ineffective. Therefore, membranous nephropathy was not completely ruled out. To our knowledge, primary membranous nephropathy is associated with a positive test for antibodies against the M-type phospholipase A2 receptor in approximately 75 to 80% of cases[4]. The patient's blood was sent for the test but revealed a negative result. As a result, before conducting a renal biopsy, we made a preliminary diagnosis of diabetic nephropathy, which is one of the most common causes of secondary nephrotic syndrome.

The renal biopsy was performed through the lower pole of the left kidney. Under sonographic guidance, four pieces of tissue approximately 0.5-1 cm in length were obtained for light microscopy, immunofluorescence, and transmission electron microscopy with hematoxylin and eosin (HE), periodic acid-Schiff (PAS) and periodic acid silver methenamine (PASM) staining. Light microscopy found mesangial hypercellularity and increased mesangial matrix with focal nodular mesangial sclerosis (Kimmelstiel-Wilson nodules). These features are diagnostic of diabetic nephropathy. Transmission electron microscopy showed glomerular basement membrane (GBM) thickening, mild foot process effacement, focal podocyte detachment, and endothelial cell swelling with a loss of fenestration (endotheliosis) without electron dense deposits. These findings are diagnostic of glomerular injury

in preeclampsia. Moreover, there were linear accentuation patterns of IgG, IgM, IgA, kappa and lambda deposition along the glomerular capillary wall as observed by immunofluorescence microscopy. With a history of preeclampsia, the diagnosis was in favor of diabetic nephropathy superimposed on the glomerular injury of preeclampsia[5] (Figure 3).

Our treatment included glycemic control and intensive blood pressure control with angiotensin receptor blockers (amlodipine/valsartan 5/80 mg once a day). During hospitalization, her body weight decreased from 90 to 70 kilograms under diuretic use. Her total urine protein/creatinine ratio decreased gradually as expected during regular follow-up after discharge.

Discussion

This 34-year-old woman with a history of type 2 diabetes and preeclampsia presented with progression of dyspnea and general edema after delivery. Pleural effusion and pericardial effusion persisted after diuretics and steroid treatment. A moderately large amount of pericardial effusion without tamponade signs was evident on an echocardiogram after admission. Pericardial effusion analysis revealed transudate effusion with no malignant cells or bacterial growth.

Pericardial effusion can not only accompany with any pericardial disease but also non-pericardial disease such as preeclampsia, nephrotic syndrome,

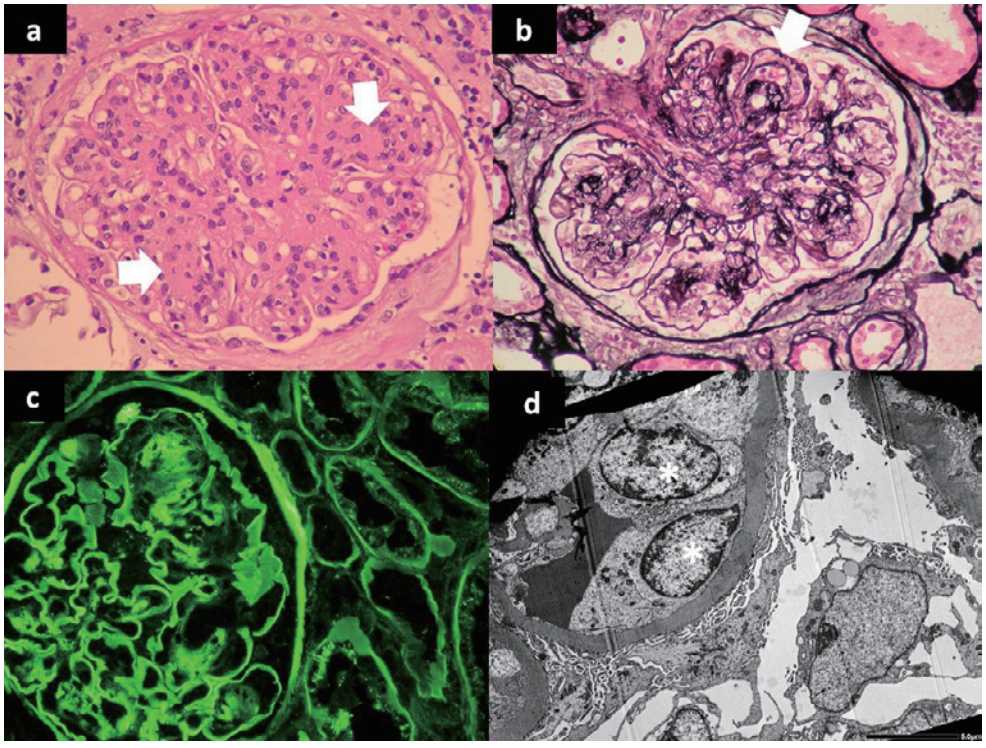

Figure 3. Light, immunofluorescence and electron microscopy images. (a) hematoxylin and eosin stains shows a representative glomerulus with Kimmelstiel-Wilson nodules(arrow) and glomerular basement membrane thickening. (b) Jones methenamine silver stains sections shows double contoured glomerular basement membrane (arrow). (c) Immunofluorescence staining with IgG shows enhancing linear staining along the glomerular basement membranes and tubules, Bowman's capsule basement membranes. (d) Electron microscopy shows uniform glomerular basement membrane thickening, mild foot process effacement, focal podocyte detachment, and endothelial cell swelling (star sign), endotheliosis without electron dense deposits.

hypoalbuminemia and even related to the side effects of the drugs. We rarely experience a case of postpartum pericardial effusion related to nephrotic syndrome superimposed on the glomerular injury of preeclampsia. To our knowledge, there is no previous report about preeclampsia with sustained pericardial effusion after delivery, and it resolved with strict control of blood pressure and serum sugar. Hypertension during pregnancy can cause pericardial effusion, although the presence of such effusions is generally asymptomatic, and no treatment is required[6]. A previous case of pericardial effusion in a woman with severe preeclampsia was reported with life-threatening complications and cardiac tamponade[7]. Fluid retention in nephrotic syndrome often leads to peripheral edema, ascites, and pleural effusions. Intuitively, pericardial effusions could be anticipated as well, but the literature is scarce regarding this complication[8]. It has been reported that an 11-year-old boy had pericardial tamponade in association with nephrotic syndrome[9], and a 45-year-old woman had nephrotic syndrome and global pericardial effusion with impending tamponade and was finally diagnosed with SLE[10]. Furthermore, methyldopa and hydralazine have been reported to be associated with drug-induced lupus erythematosus, may complicated with pericardial effusion in some cases[11,12]. Our patient had taken methyldopa for 7 days and hydralazine for 28 days in the month prior to giving birth due to hypertension. It was possible associated with pericardial effusion.

The severity of preeclampsia and the duration between the diagnosis and delivery are associated with the resolution of hypertension and proteinuria after delivery. In the natural course of preeclampsia, proteinuria usually begins to improve gradually within a few days after delivery. Sometimes, in women with several grams of protein excretion, complete resolution may take weeks to months. However, it can take up to 2 years for the hypertension and proteinuria to completely resolve[1]. In our patient, the hypertension and proteinuria persisted for 3 months postpartum. In addition, an uncommon complication-pericardial effusion-occurred. After glycemic control and intensive blood pressure control with angiotensin receptor blockers (amlodipine/valsartan 5/80 mg once a day), her body weight decreased from 90 to 70 kilograms during hospitalization, and her total urine protein creatinine ratio decreased gradually, as expected, during regular follow-up.

Conflicts of interest statement

The authors have no conflicts of interest relevant to this article.

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生產後持續的子癲前症合併嚴重心包膜積液：病例報告

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摘 要

在子癲前症的自然病程中，蛋白尿的症狀通常於生產後的幾天內緩解，若是蛋白尿症狀很嚴重，則在幾周甚至幾個月後才能完全回復。而這位病患，在生產後除了持續性地長達三個月的高血壓及蛋白尿之外，更合併了少見的併發症—心包膜積液。這位34歲女性在兩個月前成功產下了一名嬰兒，過去她有糖尿病病史長達兩年。在妊娠第二期時，因為出現嚴重蛋白尿合併高血壓的症狀，所以被診斷為子癲前症，但在生產後，心搏過速以及四肢水腫的症狀仍然持續，而且經由心臟超音波檢查發現了大量的心包膜積液，最後，腎臟切片結果是糖尿病腎病變合併子癲前症造成的腎絲球損傷所導致。子癲前症的症狀有可能在生產後持續發生，也有可能合併嚴重地心包膜積液和體液過多等症狀，良好的血壓及血糖控制即可改善蛋白尿。