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CASE REPORT

Preeclampsia or initial diagnosis of chronic renal disease during pregnancy

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Abstract: An unusual case of early nephrotic syndrome without hypertension which slightly resolved after delivery is documented. Renal biopsy was performed postpartum and the diagnosis was focal and segmental glomerulosclerosis with moderate chronic renal changes. It is questioned whether the case was due to preeclampsia or was the initial diagnosis of chronic renal disease which was made during pregnancy. The role of renal biopsy in such cases is briefly discussed *(Tab. 2, Ref. 15)*. Full Text (Free, PDF) *www.bmj.sk*.
Key words: preeclampsia, nephrotic syndrome, pregnancy, renal biopsy, focal and segmental glomerulosclerosis.

Proteinuria even up to nephrotic amounts is a common situation in pregnancy. The combination of proteinuria with hypertension in early pregnancy suggests renal disease rather than preeclampsia. Glomelural lesions associated with preeclampsia are the most common findings in pregnant renal biopsies. These changes are usually reversible. In this report, we are presenting a case of early nephrotic syndrome without hypertension which slightly resolved after delivery. Renal biopsy was performed.

Case

A 29-year-old secundigravid woman appeared instead 22 weeks of gestation with nephrotic syndrome, proteinuria (5–12 gr/24h), haematuria, but with normal renal function and blood pressure**.** At 20 weeks of gestation her 24 h urinary protein excretion was 1.25 g/24 h (V=2.5 lt). Laboratory investigation showed hct: 32.8 %, hgb: 11 g/dl, MCV: 89, urea: 14 mg/dl, creatinine: 0.5 mg/dl. The clotting was normal. At 22nd week of gestation her laboratory investigation showed hgb: 11.3 gr/dl, hct: 32.2 %, MCV: 93.2, WBC: 8.6 k/ml, platelets: 398500 k/ml, total proteins: 4.0 g/lt, fibrinogen: 637.9 mg %. Her 24 hour urinary protein excretion was up to 350 mg/24h. The routine ultrasound scan of the fetus at 22 weeks was reported as a single fetus without any anomalies. Amniotic fluid was normal. At 24 week plus 2 days of gestation platelets elevated up to 431700 k/ml and urea up to 11 mg/dl. Creatinine was 0.45 mg/dl and total proteins wereas 3.9 gr/dl and fibrinogen: 605.9 mg%. The 24 h urinary protein excretion was 180 mg/24 h. At 27 week plus 2 days of gestation platelets were up to 417200 k/ml and urea up to 24 mg/dl. Creatinine was 0.51 mg/dl and total proteins wereas 4.3 gr/dl and fibrinogen: 396.1 mg %. The 24 h urinary protein excretion was 300 mg/24h. Doppler ultrasound scan was normal. Bed rest was advised. Vaginal delivery took place at 38 weeks plus 4 days of gestation. Postpartum she was closely followed up. Four months postpartum the tests were the following: fibrinogen: 550 mg %, platelets: 458 000/ml, total proteins: 4.04 g%, albumins: 1.84 g%, normal levels of urea, creatinine, but 24 h urinary protein excretion was up to 4.7 g/24 h (V=2460 ml). Clinical urinalysis showed proteinuria >300 mg/dl. Five months after the delivery she visited a renal clinic because of facial and lower limb oedema. The blood pressure was in normal levels. Proteinuria (>3 gr/dl) was found with normal renal function and moderate microscopic haematuria of glomerulonephritis type. Her 24h urinary protein excretion was 11.9 g (V=3lt). Clinical urinalysis showed proteinuria: +++. Laboratory investigations showed serum sodium: 139 mEq/lt, potassium: 4 mEq/lt, urea: 18 mg/dl, creatinine: 0.7 mg/dl, albumin: 2.6 g/lt, haemoglobin: 13.6 gr/dl, haematocrit: 40.2 %. After transabdominal ultrasound scan normal renal size and morphology was found. After renal biopsy the diagnosis was focal and segmental glomerulosclerosis with moderate chronic renal changes. On her release exit from the renal clinic, she was ordered for low salt diet, every day weight measuring, sodium and potassium screening and renal follow up. Six months after the delivery her clinical status was clear.

Discussion

Hypertension and proteinuria during pregnancy is the combination which is defined as preeclampsia (1). An elevation above 140 mmHg systolic or 90 mmHg diastolic for women without history of chronic hypertension meets the criteria (2). 300 mg or more of protein in a 24-hour urine collection is defined as pro-

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teinuria. Furthermore, facial oedema and oedema of the hands and feet is a minor criterion of the diagnosis, as many pregnant women with normal blood pressure have these types of such an oedema. Other signs and symptoms that may be present in preeclampsia are headaches, visual disturbances, epigastric pain, elevated liver enzymes, elevated or decreased hematocrit, and decreased platelets (3). Preeclampsia occurs in 6–8 % of all live births. Nulliparity, extreme maternal ages (<15 and >35 years of age), African-American race, diabetes, chronic vascular or renal disease, chronic hypertension, multiple gestations, and history of preeclampsia in a prior or a first degree female relative's pregnancy are the risk factors of preeclampsia (4).

There are many theories (5, 6) which try to explain the mechanism of preeclampsia such as the theory of immunologic response, the role of circulating toxins, the role of endogenous vasoconstrictors, the theory of endothelial damage and the theory of the primary disseminated intravascular coagulation. Preeclampsia seems to be a damage of the placenta rather than the kidney. There is a 25 % chance of preeclampsia recurrence in subsequent pregnancies especially in women who develop severe or early in pregnancy preeclampsia or in women with a history of chronic hypertension or renal disease. Preeclampsia does not increase the risk of hypertension later in maternal life. The classification of preeclampsia is mild or severe. The criteria which classify a preeclampsia as severe are the following: systolic blood pressure >160 mmHg or diastolic blood pressure >110 mmHg on two occasions at least 6 hours apart, proteinuria >5 g/24 h, oliguria <500 cc/24 h, cerebral or visual symptoms, epigastric or right upper quadrant pain, pulmonary oedema or cyanosis, low platelets, elevated liver function tests and fetal growth restriction. Mild preeclampsia is any preeclampsia that is not considered severe.

On the other hand, the initial diagnosis of chronic renal disease in women with no other medical problems may be made during pregnancy (7). Renal disease may be silent in early stages. At first prenatal visit, a urine analysis is performed. In suspicion, a 24-hour urine collection for total protein and creatinine clearance should be performed. Total protein excretion should be <0.3 g/day. Creatinine clearance can decrease about 70 % before an elevation in serum blood urea, nitrogen or creatinine (Tab. 1).

The long-term effects of pregnancy on renal disease are unclear. Creatinine clearance will still elevate in women with baseline dysfunction. Near pregnancy completion, creatinine clearance falls in patients with underlying renal disease, a fact that reverses after delivery. In cases with mild renal disease (serum creatinine <1.4 mg/dl), renal function is not worsened by pregnancy, but there is an increased risk for pyelonephritis. Deterioration of renal function that may not improve after delivery may appear in women with moderate to severe renal insufficiency (serum creatinine >1.4 mg/dl and <2.5 mg/dl). Hypertension and diabetes can also raise the risk for irreversible renal disease with pregnancy.

Tab. 1. Intrinsic renal disease versus preeclampsia.

	Renal disease	Preeclampsia
Serum creatinine	>1.0 mg/dL	0.8–1.2 mg/dL
Urinary protein	Variable	>300 mg/d
Uric acid	Variable	>5.5 mg/dL
Blood pressure	Variable	>140/90 mmHg
Liver function test results	Normal	May be increased
Platelet count	Normal	May be decreased
Urine analysis	Variable	Protein, with or without erythrocytes, leukocytes

Tab. 2. Causes of proteinuria.

Glomerular
- Primary glomerulonephropathy
- Minimal change disease
- Idiopathic membranous glomerulonephritis
- Focal segmental glomerulonephritis
- Membranoproliferative glomerulonephritis
- IgA nephropathy
- Secondary glomerulonephropathy
- Diabetes mellitus
- Collagen vascular disorders (e.g., lupus nephritis)
- Amyloidosis
- Preeclampsia
- Infection (e.g., HIV, hepatitis B and C, poststreptococcal illness, syphilis, malaria and endocarditis)
- Gastrointestinal and lung cancers
- Lymphoma, chronic renal transplant rejection
- Glomerulonephropathy associated with the following drugs:
  - Heroin
  - NSAIDs

Glomerular (continued)
- Gold components
- Penicillamine
- Lithium
- Heavy metals

Tubular
- Hypertensive nephrosclerosis
- Tubulointerstitial disease due to:
- Uric acid nephropathy
- Acute hypersensitivity interstitial nephritis
- Fanconi syndrome
- Heavy metals
- Sickle cell disease
- NSAIDs, antibiotics

Overflow
- Hemoglobinuria
- Myoglobinuria
- Multiple myeloma
- Amyloidosis

Nephrotic syndrome occurs in 0.012–0.025 % of all pregnancies (8). The incidence of pregnancy induced hypertension is 3 % and eclampsia is 0.1 %. Nephrotic syndrome (3.5 g protein/ /24 h) may be caused by diabetes, systemic lupus erythematosus, renal vein thrombosis, amyloidosis, minimal change disease, membranous glomerulonephritis and membranoproliferative glomerulonephritis. However, the most common reason is preeclampsia. Generally, few problems are caused by nephrotic syndrome in pregnancy if there is not hypertension or renal failure (9). Physiological changes during pregnancy may cause a diagnostic dilemma as they mimic exacerbation of the disease. In pregnancy, the normal urinary protein excretion is elevated to 0.39 g/day, the serum albumin is reduced by 5–10 g/l. Further

reduction of serum albumin due to nephrotic syndrome can cause fluid retention (Tab. 2).

Investigation of the cause of renal disease during pregnancy can be conducted with serologic, functional, and ultrasonographic testing. Renal biopsy is rarely performed during gestation. Renal biopsy usually is reserved for situations in which renal function suddenly deteriorates without apparent cause or when symptomatic nephrotic syndrome occurs, particularly when azotemia is present. Almost no role exists for renal biopsy after gestational week 32 because at this stage the fetus will likely be delivered, independent of biopsy results. Before starting treatment, it is important to know the histology as sometimes nephrotic syndrome does not respond to steroids (10). Renal biopsy with subsequent pathologic classification is a technique which showes the effect of renal disease on pregnancy and vice versa. Lindheimer and Davison (11) in 1987 and Lindheimer and Katz (12) in 1994 believed that although renal biopsy during gestation has no increased risks, it should be infrequently performed in pregnancy. The indications of its use are sudden renal insufficiency or massive nephrotic syndrome of unknown origin occurring prior to the final two months of pregnancy. However, mild or moderate proteinuria in normotensive patients with well preserved renal function should be closely monitored and the renal biopsy should be performed after delivery. Contrary to a previous report by Weisman et al (13), Fisher et al (14) showed in their retrospective report that 67 % of the renal biopsies showed preeclamptic changes and one-third of them had nephrotic range proteinuria, and so they concluded that nephrotic range proteinuria is common in preeclampsia, but despite this, recovery was complete in most instances. Criscuolo et al (10) believed that it was necessary to investigate whether the nephrotic syndrome was evidence of an underlying nephropathy or was just a result of preeclampsia. The suggested treatment was rest, control of blood pressure, correction of low blood volume and delivery of the fetus with regard to its maturity and viability. After delivery, all signs cleared up, and all women were cured in six months. Renal dysfunction, hypertension and oedema resolved in the postpartum period (14). Shiiki et al indicated that focal and segmental glomerulosclerosis might not only be induced by preeclampsia but also be one of the representative glomerular changes in preeclamptic women with nephrotic syndrome. Gartner showed that the severity of the glomerular lesions correlated with the proteinuria, hypertension and nephrotic syndrome (9). Furthermore, hypertension also correlated with mesangial and subendothelial deposits and with focal segmental hyalinosis and sclerosis. A morphometric analysis of the ultrastructural changes in the glomerulus in preeclampsia showed that subendothelial fibrinoid deposits were a significant feature of biopsies during pregnancy, but disappear in the postpartum period. On the other hand, capillary wall changes with reduplication of glomerular capillary walls and mesangial interposition may exist till 18 months after delivery (15). Foam cells in glomeruli are rarely found in biopsies during pregnancy, but appear during resorption of the subendothelial deposits in the postpartum period. Segmental lesions may appear during preeclampsia and disappear after pregnancy.

Conclusion

In our case report, it is questioned whether the case was due to preeclampsia or was the initial diagnosis of a chronic renal disease which was made during pregnancy. The necessity of the correlation between an early nephrotic syndrome and hypertension is also discussed. Finally, the role of renal biopsy in such a case is presented. Further studies are necessary to be made in order to investigate the role of hypertension in the diagnosis of early nephrotic syndrome.

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