Spectrum of Renal Lesions Seen in Patients Who Had a Recurrent Preeclamptic Disorder in Their Subsequent Pregnancies

TEKRARLAYAN PREEKLAMPSI OLGULARINDA BÖBREK L EZ YO NLA RININ DEĞERLENDİRİLMESİ

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Summary

Objective: To evaluate the renal lesions seen in the patients who had a recurrent preeclamptic disorder in their subsequent pregnancies and to asses the correlation between the histological type of lesions and the severity of the renal disease.

Institution: Istanbul University Istanbul Medical Faculty, Department of Internal Medicine and Department of Obstetrics and Gynecology.

Material and metods: 34 women with the signs of severe preeclampsia during their previous pregnancies, have been studied. Kidney functions were determined by GFR and urea clearance. Renal biopsies were done within three month, after delivety if there are the hypertensive disorders or/and proteinuria after this time. All tissues were processed for examination under light microscopy.

Results: Among 34 patients with the clinical sign and symptoms of toxemia a biopsy diagnosis of underlying glomerulonephritis had been made in 20 cases (58 %), chronic pyelonephritis in 6 cases (18 %) and pure preeclamptic toxemia in 8 cases (24%). Mesangioproliferative nephropathia have been found to be the most common histological lesions seen in both pure toxemia (87%,) and chronic renal lesions (60%,).

Conclusion: Mesangioproliferative nephropathia was found to be the most common renal lesions seen in both pure toxemia and chronic renal disease. Significance of constellation of clinical, laboratory and histological findings in making the find diagnosis have been emphasized.

Key Words: Toxemia, Chronic renal disease, Mesangioproliferative nephropathia

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Özet

Amaç: Daha önceki gebeliklerinde de preeklampsi geçiren olguların böhreklerindeki patolojiyi saptamak ve böbrek hasarının şiddeti ile lezyomın histolojik tipi arasındaki ilişkiyi araştırmayı amaçladık.

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*Materyal-**Metod:** Daha önceki gebeliklerinde de preeklampsi geçirmiş olan ve doğumdan sonraki üç ay içinde remil patolojileri devam eden 34 preeklanıptik olgu çalışına grubumuzu oluşturdu. Hastaların böbrek fonksiyonları glomerüler flitrasyon hızı ve üre klirensi ölçülerek değerlendirildi. Böbrek biyopsileri doğum sonrası üç aylık period içinde, renal patolojinin devamı durumunda yapıldı ve histopatolojik değerlendirme ışık mikroskobunda değerlendirilerek gerçekleştirildi.*

***Bulgular:** Klinik tanı olarak: 20 olguda (%58) gloınerıdonefrit, altı olguda (%I8) kronik piyeloıiefrit ve sekiz olguda sadece preeklamptik tokseuui saptandı. Mezangioproliferatif nefropati hem sadece preeklampsi saptanan, hemde kronik renal lezyoıı bulunan olgularda, en fazla görülen histopatolojik tanı oldu.*

Sonuç: Doğum sonrası renal patolojileri devanı eden preeklamptik olgularda en sık görülen histopatolojik tanı "Mezangiopro/iferatif Nefropati" olarak belirlendi. Tanıda klinik, laboratuar ve gerekirse histopatolojik tanının önemi vurgulandı.

Anahtar Kelimeler: Toksemi, Kronik renal hastalık, Mezangioproliferatif nefropati

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Hypertensive disorders are the most common medical complication of pregnancy. Approximately 5-10 % of all pregnancy are complicated by hypertension.(l). In 1986, The American College of Obstetricians and Gynecologists Committee pub-

lishcd the definition of hypertension in pregnancy: A systolic pressure more than 140 mm Hg. or an increment more than 30 mm Hg. for the systolic pressure from the baseline of blood pressure in the first half of pregnancy or a diastolic pressure more than 90 mm Hg. or an increment more than 15 mm Hg. for the diastolic pressure from the baseline.(2). Preeclampsia, defined as a hypertension together with abnormal edema or proteinuria. But; High blood pressure, proteinuria and edema during pregnancy may be due to preeclamptic toxemia or underlying renal disease.

Because this is the most common medical complication of pregnancy there arc many research and publication about the hypertensive disorders. Most authors claim that there are specific morphological changes in the kidneys of woman with preeclampsia described as glomerular capillary endotheliosis. These lesions have been found to be reversible. (3,4,5). However, the appearance of such lesions during pregnancy does not preclude the presence of an underlying glomerulonephritis with superimposed toxemia.(5,6). We do not now the essential reason of maladaptation of preeclamptic woman. In pregnant patients with subclinical glomerulonephritis, relatively minor changes may occur in glomeruli and the changes resulting from preeclamptic toxemia may mimic those of glomerulonephritis. Therefore differential diagnosis may be difficult. Other condition such as pyelonephritis was frequently confused with toxemia. So many persons referred to a clinic for so called toxemia had hypertensive vascular disease and pyelonephritis. (7-10).

On the other hand, type of the renal pathology and the type of the preeclampsia is very important for the prognosis of the patient. The renal pathology is reversible generally and the hypertension return to the normal level or can be controlled control with some medication after delivery. If the reversibilty symptoms does not occur by six weeks, a work up to assess hypertension should be performed. For the proteinuria, this time is one week and proteinuria usually recedes within 1 week after delivery. But exceptional cases the protein leak may take more than 1 month to heal. In superimposed preeclampsia, renal functions usually may not improve after delivery. This is the important point for the prognosis of the patient. If there is a hypertensive disorder or proteinuria after birth, it is very important to make pathological diagnosis of toxemia and the severity of the histopathological renal destruction for accuracy and reliability of the prognosis (11). And there are some questions in our mind: What arc the main morphological features in our preeclamptic patients in their repeated pregnancies ?, How these morphological findings are subsequent to the clinical findings?.

The aim of this study is the examination of the histopathological proofs of renal destruction as well as answering these questions in hypertensive disease in pregnancy.

Materials and Methods

34 women who had a recurrent preeclamptic disorder in their subsequent pregnancies and renal disorders after birth, constituted our materials. The diagnosis of preeclampsia based on the criteria's of The American College of Obstetricians and Gynecologists committee.

Firsts, we classified clinicopathologically this patients in three category:

1. Chronic pyelonephritis
2. Chronic glomerulonephritis
3. Pure preeclamptic toxemia

After that, we evaluated the renal functions by urea clearance and glomerular filtration rate during pregnancy and six weeks after delivery if these patients had a high blood pressure, proteinuria or both until this time. At the same time, the blood urea and creatinin determinations of these patients has been done by Technicon SMA60 and SMA12 system autoanalysis.

We performed 34 percutaneous renal biopsies to these patients under local anesthesia. Biopsies were carried out to determine the nature of underlying renal disease and to asses the severity of lesions. All tissues were processed for light microscopy. Because the same histologic type of renal lesions can be seen in different clinical features, the classification of the glomerulonephritis and making an correlation between the pathological lesions and clinical features is very difficult. Pathological results of the renal biopsies and clinical findings were classified according to Renec Habib (12).

Results

The average ages of the patients were 26.5 ± 3.2. A11 the patients have the criteria for the diagnosis of severe preeclampsia. A11 of them had a proteinuria more than 5000 mgr. and all of the patients had a systolic pressure above 160 mm Hg. and/or a diastolic pressure above 110 mm. Hg. There was no difference at the initial hematological parameters of the patients, like PTT, PT, platelets or SCOT.

Among 34 patients with the clinical sign and symptoms of toxemia, a biopsy diagnosis of underlying glomerulonephritis had been made in 20 cases (58%), chronic pyelonephritis in 6 cases (18%) and glomerular capillary endotheliosis (pure preeclamptic toxemia) in 8 cases (24%) (Table 1).

A11 26 patients (76%) with underlying chronic glomerulonephritis and pyelonephritis were found to have persisting clinical findings, urine abnormalities and impaired renal functions after pregnancy which confirmed the diagnosis. In this patients the mean G F R (Glomerular Filtration Rate) were found to be about 80.72 ¿13.24, ml/mm during pregnancy and 70.69 ± 3.22 ml/min after delivery. Urea clearance were about 39.72 ± 8.36 ml/min during pregnancy and 29.50 ± 1.58 ml/min after delivery. In this groupe, the decline of the mean G F R and urea clearance were statistically significant ($p<0.001$, $t=5.65$; $p<0.001$, $t=6.89$). In the other group who had a pure preeclamptic toxemia, the results of G F R and urea clearance showed the return of normal renal functions and disappearance of urinary function abnormalities and clinical findings. In this group of patients the mean G F R was found to be 108.86 ± 15.80 ml/min during pregnancy and 125.23 ± 2.35 ml/min after delivery. Urea clearances were 49 ± 6.54 ml/min and 54 ± 5.04 ml/min after delivery (Table 2). The difference and increase of the values before and after delivery were statistically significant in the pure preeclamptic toxemia group as well ($0.001<p<0.01$, 1=3.87, O.OOK p O.O1, t=3.87).

In patients with glomerulonephritis, biopsy revealed 12 (60%) to have mesangioproliferativc glomeulonephritis, 5 (25%) to have membronoprolipherativc lesions. Whereas in patients with pure preeclamptic toxemia 7 cases (87%) showed mesangioproliferative lesions and only one ease (%12) had membranoproliterative changes. In six patients toxemia was found to superimposed to a biopsy proven chronic pyelonephritis (Table 3).

Table 1. Distribution of cases

Clinicopathological Findings	Number	%
Chronic glomerulonephritis	20	58
Chronic pyelonephritis	6	18
Pure preeclamptic toxemia	8	24
TOTAL	34	100

Discussion

Hypertensive disorders arc the most common medical complication of pregnancy. The effects of this complications usually return to normal after delivery. If this change docs not occur by six weeks, a workup to assess hypertension should be performed. The majority of women with preeclampsia have mild to moderately diminished renal perfusion and glomerular filtration with correspondingly elevated plasma creatinine and uric acid levels. This clinical view causes some mistake in the diagnosis of this illness. Cheslcy (4) has pointed out the likely errors in diagnosis of preeclampsia (11). These are: (i) the patient might have latent hypertension which is revealed by preg-

Table 2. Results of renal functions tests before and after labor

	GFR			Urea Clearance		
Renal Disease	Pregnancy	After Delivery	p	Pregnancy	After Delivery	p
Chronic Glomerulonephritis and chronic pyelonephritis	80.72±13.24	70.69+3.22	pO.001 t=5.65	39.72+8.36	29.5011.58	pO.001 t=6.89
Pure preeclamptic toxemia	108.861145.80	125.23+2.35	0.00 K p <0.01 t=3.87	49.41 ±6.54	54.9515.04	0.00 K p <0.0 1 t=3.S7

Table 3. Distribution of cases with respect to their histopathological appearance

Disease	Number	%	Total
Chronic Glomerulonephritis			20
1. Mesangioproliferative	12	60	
2. fvl embranopro l i ferati ve	5	25	
3. Simple proliferative	3	15	
Pure Preeclamptic Toxemia			8
1 .Mesangioproliferalive	7	87	
2. Ivl embranopro l i ferati ve	1	12	
Chronic Pyelonephritis			6
TOTAL			34

nancy; (ii) chronic glomerulonephritis or other renal disease is present; (iii) the is suffering from essential hypertension which has abated during pregnancy. This error may be particular source of confusion since preexisting hypertension may fall during the second trimester only to rise again during last three months. Apparently the greatest difficulties are confronted when lacking of the data about the patient status before pregnancy.

Me Cartney noted that 25 percent of 63 primipars diagnosed clinically as having preeclampsia did not have preeclampsia. Most of the misdiagnosis were in patient with chronic glomerulonephritis. (3,11) Similarly Fisher (13) using renal biopsies claimed that preeclampsia could be misdiagnosed on clinical grounds. Robson (8) summed up the situation by pointing out "The structural lesions in preeclampsia characteristic only in the sense that a number of individual components of glomerular injury which are themselves commonly seen in other glomerular disorder occur in particular balance and not because of any single unique or specific feature". It is equally true that most conditions are diagnosed by configuration of findings. However difficulties could arise differentiating the lesions in glomerulonephritis from those of preeclamptic toxemia because changes in pure preeclamptic toxemia may mimic those seen in glomerulonephritis. Same type of lesions might be seen in both toxemia and glomerulonephritis.

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 were absent in many biopsies in the postpartum period. These deposits disappear progressively in the first week after delivery. Capillary wall changes with reduplication of glomerular capillery walls and mesangial interposition are another prominent feature of preeclampsia. Foam cells in glomeruli arc rarely found in biopsies during pregnancy, but appear during resorption of the subendothelial deposits in the postpartum period(14). Electron-dense droplets in glomerular epithelial cells are a characteristic feature of preeclampsia. Immunogold labeling demonstrates that they contain albumin, immunoglobulins, fibrinogen, and complement. Fibrinogen is usually present in an inner electron-dense core in a droplet. Other proteins are diffusely distributed. Segmental hyalinosis is a change that closely resembles the changes of preeclampsia, and segmental lesions may appear during preeclampsia and disappear after pregnancy(14). Renal biopsy specimens taken from preeclamptic patients are found to be associated sometimes with focal segmental glomerular scelerotic lesions that closely resemble those of primary focal segmental glomeruloscelerosis (15).

In our study mesangioproliferative changes have been found to be the most common histological lesion seen both in toxemia and glomerulonephritis. But it is more common in toxemia (87%) than in glomerulonephritis (56%). Therefore increased mesengial prominence might be accepted as a feature of pure preeclamptic toxemia only if it is supported by clinical findings and renal functions. Clinical findings and renal function as were in our cases should return to normal before pregnancy states. Similar results were obtained by Seymour (17). In his series renal biopsies from 14 patients with active preeclamptic toxemia, revealed that the glomeruli were diffusely enlarged with prominent lobulation and reduction in vascular spaces. This reduction was pronounced principally by longitudinal mesengial expansion which encroached upon capillary lumina and which was associated with wide spread mesangial interposition (double countours) in PASM stain. There was no leucocytic inflitration. Endothelial swelling was variable and rarely pronounced, but endotelial mesangial foam cells were present in six patients. Kinkaid Smith also had similar results obtained from 123 patients with renal biopsies. (14,15).

On the other hand, focal segmental scelerosis has been found to be the most striking feature in preeclampsia. In fact tubulo interstitial lesions such as tubular atrophy, interstitial fibrosis and lymphocytic infiltration were thought to be an important prognostic factor in preeclampsia, and unequal dilatation of glomerular capillaries in non-scelerotic glomeruli has been held responsible from the development of glomerular scelerosis (16).

As to the spectrum of renal lesions seen in our patients who have signs of recurrent toxemia in their subsequent pregnancies, glomerulonephritis was found to be the first (with 58%), pure preeclamptic toxemia the second (24%), and chronic pyelonephritis to be the third (18%) common lesions. These results concur with literature (17-19).

As a conclusion it can be said that the mesangioproliferative nephropathia is the most common histological lesion seen in both pure toxemia and in underlying chronic renal disease with superimposed toxemia. Therefore it is very difficult to differentiate these 2 diseases (pure toxemia from underlying renal disease) solely by their histological appearances. Clinical findings and renal functions should be followed up, and final diagnosis should be made by constellation of clinical, laboratory and histological findings.

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