

A Case of Crescentic Glomerulonephritis That Developed After Marijuana Use

Esrar Kullanımı Sonrası Gelişen Kresentik Glomerulonefrit Olgusu

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ABSTRACT Rapidly progressive glomerulonephritis (RPGN) is a rare entity and characterized by rapid deterioration of renal functions within weeks or months. Drug abuse is a well known cause of some renal pathologies which are nephrotic syndrome, acute glomerulonephritis, interstitial nephritis and rhabdomyolysis. In this paper we present a case of rapidly progressive glomerulonephritis that developed after marijuana use that is unique in literature.

Key Words: Marijuana abuse; substance-related disorders; glomerulonephritis

ÖZET Hızlı ilerleyen glomerulonefrit böbrek fonksiyonlarının haftalar veya aylar içinde bozulması ile karakterize nadir bir antitedir. Uyuşturucu madde kullanımının bazı glomeruler patolojilere yol açabildiği bilinmektedir. Nefrotik sendrom, akut glomerülonefrit, interstisyel nefrit ve rabdomiyoliz bunlar arasında yer alır. Biz de bu makalede daha önce literatürde rastlanmayan, esrar kullanımı sonrası gelişen kresentik glomerulonefrit vakasını sunmaya çalıştık.

Anahtar Kelimeler: Marihuana kullanımı; madde kullanımına bağlı bozukluklar; glomerulonefrit

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Most of the glomerular diseases are idiopathic. Clinical presentation of glomerular diseases may range from merely hematuria or proteinuria to nephrotic or nephritic syndrome.¹ Rapidly progressive glomerulonephritis (RPGN) is characterized by rapid deterioration of renal function (50% or more decline in the glomerular filtration rate (GFR) within 3 months) and extensive crescent formation seen in at least 50% of glomeruli seen in kidney biopsies. So RPGN is also called crescentic glomerulonephritis.² Early diagnosis and treatment plays a key role in the prognosis of RPGN, so RPGN should be differentiated from other glomerular diseases which have similar symptoms and urinary signs. The appropriate treatment strategy for crescentic glomerulonephritis varies depending on the immunopathologic category and disease severity at the time of presentation.^{3,4} If left untreated, most of the cases develop end stage kidney disease in a few weeks or months.

In this paper we aim to present a case of RPGN associated with marijuana use. This is the first case report of RPGN associated with marijuana use

in literature. Informed patient consent for publication was obtained.

CASE REPORT

A 21-year-old female patient admitted to our hospital with symptoms of arm and leg swelling for the past 2 months. She had no history of any regular drug use or chronic disease. Family history was negative for renal diseases. Recent nephrotoxic drug use was not realized. On physical examination diffuse edema which was more prominent at periorbital and pretibial regions was detected. Blood pressure was 150/90 mmHg and heart rate was 78 beats per minute. Other systemic examinations were normal. Admittance laboratory results were as follows; urea: 80 mg/dL, creatinine: 3.6 mg/dL, Ca: 7.3 mg/dL, P: 5.3 mg/dL, Hb: 10.5 g/dL, Htc: 31.9%, MCV: 82.8. Urine sample was evaluated with strips and the results were as follows; protein +3, erythrocyte +3, leukocyte +1. 24 hour urine protein was calculated as 6.8 g. Microscopic hematuria, nephrotic range proteinuria, and normal kidney function tests those runned 2 months ago evoked suspicion of rapidly progressive glomerulonephritis and the patient was hospitalized. Ultrasonographic measurement of long and short axes of renal parenchyma were 110 mm and 18 mm in right kidney; 113 mm and 18 mm in left kidney respectively. Ecogenities were normal.

Differential diagnostic tests were carried out and the results were as follows: negative for ANA, p-ANCA, c-ANCA, HBS ag, anti-HIV, anti-HCV and positive for anti HBS ag; parathormone: 153 pg/mL, 25 OH vitamin D level < 3 ng/mL, total protein: 4.9 g/dL, albumin: 1,7 g/dL, C3 was normal, C4 was increased 2 fold above the upper limit of normal. Ultrasound assisted kidney biopsy was performed. Light microscopy showed diffuse crescent formation in all glomerulus but necrosis was not present (Figure 1). Interstitial mixed type inflammatory infiltration which was composed of neutrophils and a few eosinophils was seen (Figure 2). Vascular endothelial proliferation was seen but no fibrinoid necrosis was detected which would suggest vasculitis (Figure 3). Mild tubular necrosis was realized. Immunofluorescence microscopy detected

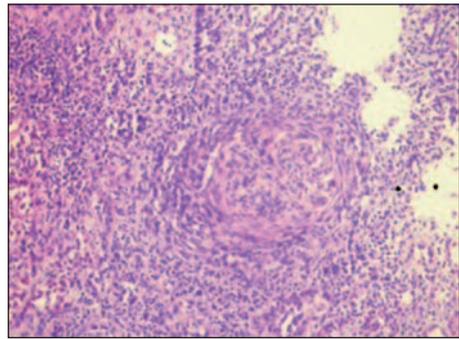


FIGURE 1: Cellular crescents on glomerulus and diffuse tubulointerstitial inflammation (HE, X200).

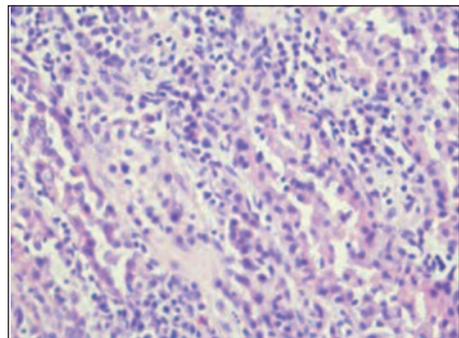


FIGURE 2: Mixed type inflammation also containing eosinophils at tubulointerstitial area (HE, X400)

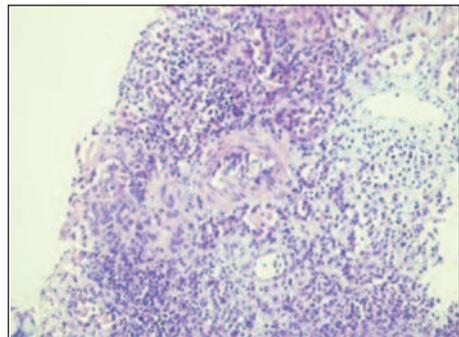


FIGURE 3: Marked endothelial proliferation in vessel walls (HE, X200).

no complement or immunoglobulin on glomerulus and vessels. By the light of biopsy findings the case was diagnosed with crescentic glomerulonephritis. Anti glomerular basal membrane test was negative. Further anamnesis revealed that the patient had been using narcotic drugs of varying types and doses for a long time and had been using marijuana until 1 month ago. Also she used high dose progesterone for voluntary abortus 2 months ago. After

definitive diagnosis the patient was treated with intravenous pulse steroid (1 g/day, for 3 days) and intravenous cyclophosphamide (500 mg/m²). Oral prednisolone (1 mg/kg/day) followed the first treatment and no adverse effects were seen during treatment period. Follow-up showed no recovery in kidney function tests so plasmapheresis was planned but the patient rejected this treatment modality, so it was cancelled. Outpatient clinic appointment was planned and the patient was discharged. Pre-discharge urea was 224 mg/dL, creatinine was 5.5 mg/dL. First month control urea was 193 mg/dL, creatinine was 6.3 mg/dL, creatinine clearance was calculated as 17 mL/24 hour.

DISCUSSION

In the last 30 years, the number of people using narcotic drugs appears to have increased. Currently, substance abuse is growing among adolescents worldwide.⁵ Recent evidence suggests more than 40% of young people have tried illicit drugs at some time.⁶ Commonly abused drugs are alcohol, opiates, sedatives, hypnotics, cocaine, marijuana, hallucinogens and amphetamine. These drugs and their metabolites are eliminated from body mostly by kidney route. It is well known that narcotic drug use causes various kidney diseases. The renal complications of drug abuse are also becoming more frequent, and may encompass a spectrum of glomerular, interstitial and vascular diseases. Some of these drugs are nephrotoxic. Mostly they cause renal damage by unknown mechanisms.⁶ Kidney failure seen in drug addicts is associated not only with drug effects but also with socioeconomic status, culture, habits and genetic tendency of patients.⁷ Kidney damage caused by cocaine and heroin can be seen in forms of nephrotic syndrome, acute glomerulonephritis, secondary amyloidosis, interstitial nephritis and rhabdomyolysis.⁶ Most frequent lesion caused by heroin use is focal segmental glomerulosclerosis in blacks, and membranoproliferative glomerulonephritis in whites.⁷ Heroin damages kidneys either by immune complex deposition or by glomerular fibroblast proliferation.⁸ Infections caused by frequent intravenous injections among heroin users may be the real cause of

glomerulonephritis.⁹ It is well known that cocaine use may lead to renal failure by causing rhabdomyolysis.¹⁰ It may also cause renal infarcts and atherosclerosis. Marijuana is a dry, shredded green and brown mix of leaves, flowers, stems, and seeds from the hemp plant *Cannabis sativa*. Marijuana is the most common illicit drug used in the United States but data suggesting that marijuana may damage kidneys were limited.¹¹ Literature showed a case of membranous glomerulonephritis in a patient who used high dose marijuana for a long time after renal transplantation.¹¹ Renal infarct developed in a case using marijuana.¹² Beyond renal infarct, renal problems associated with marijuana use are acute tubular necrosis, tubulointerstitial nephritis and mesangioproliferative glomerulonephritis.^{13,14} But no case of crescentic glomerulonephritis which is associated with marijuana use was published.

Rapidly progressive glomerulonephritis (RPGN) is generally seen in 5th decade of life and more common among male patients. Hypertension, edema, oliguria are among the frequent findings.³ Cases associated with systemic diseases show more insidious presentation with arthritis, fatigue and fever, but sometimes may also present as acute glomerulonephritis. Renal failure is common and serum creatinine level is generally above 3 mg/dL. Microscopic urinalysis reveals various degrees of proteinuria, erythrocyte cylinders and dysmorphic erythrocytes. Although microscopic urinalysis, by revealing red cells and granular casts, is more specific, simple stick testing is also highly sensitive.¹⁵ Causes of rapidly progressive glomerulonephritis are Good pasture syndrome, anti GBM nephritis, IgA nephropathy, lupus nephritis, membranoproliferative glomerulonephritis, acute poststreptococcal glomerulonephritis, Wegener glomerulonephritis, Churg-Strauss syndrome and microscopic polyangitis.

In our case, we detected progressive kidney failure which had developed within 3 months of time. With the initial diagnosis of rapidly progressive glomerulonephritis, we performed kidney biopsy which showed crescentic glomerulonephritis. More tests were performed for differential diagnosis but none of them were positive for a cause

of crescentic glomerulonephritis. ANCA related vasculitic lesions were eliminated, hepatitis and HIV serology were detected as negative, and anti GBM antibody was detected as negative. No history of hemoptysis and no positive sign in chest X-rays eliminated the possibility of Good pasture syndrome. Lupus nephritis was eliminated with the results of ANA and anti ds-DNA negativity. Long term marijuana use in history was suggested as the cause of renal damage. Again literature has no data about a probable association between high dose progesterone that the patient used and nephrotoxicity. Unresponsiveness to pulse steroid and cyclophosphamide therapy is also thought to be

consistent with a non vasculitic and non immune complex disease. Recently, new therapeutic agents have emerged, such as monoclonal antibodies to T cells, B cells and cytokines (e.g. anti-CD20 antibodies and TNF- α inhibitors) and signal transduction inhibitors, which may provide satisfactory alternatives.¹⁶ We do not have enough data to answer the question of “By which mechanism marijuana caused renal damage?” so new studies are required to answer this question.

In conclusion drug abuse should be kept in mind as a rare cause of idiopathic crescentic glomerulonephritis, and the patient should be questioned about it.

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