Anti-dsDNA Positivity in a Patient with Prostate Cancer and Acute Kidney Injury: A Case Report

Akut Böbrek Hasarı ve Prostat Kanserli Olguda Anti-dsDNA Pozitifliği: Olgu Sunumu

ABSTRACT

OBJECTIVE: Patients with malignancies may develop autoimmune and rheumatic manifestations as a result of generation of autoantibodies, paraneoplastic syndromes, direct invasion of joints and muscles by the tumour cells, or combination chemotherapy. We present a case with prostate cancer and acute kidney injury (AKI) mimicking rapidly progressive glomerulonephritis with a positive test result for anti-double-stranded deoxyribonucleic acid antibodies (Anti-dsDNA ab).

CASE PRESENTATION: The 78-year-old male patient applied to our center with the complaint of generalized bone pain since approximately two months, and rapid onset of weakness, oliguria and dysuria for three days. He had been diagnosed metastatic prostate cancer (PC) for two years and at the time of application had received high dose of naproxen sodium because of severe bone pain for 5 days. Serum creatinine level was elevated on admission (2.4 mg/dl). Urinalysis revealed microscopic hematuria, granular casts and proteinuria of 1.2 gr/day. Immunologic tests including Anti-dsDNA antibody were done regarding acute nephritic syndrome. The subject was positive for Anti-dsDNA ab with a value of 96 IU/ml (normal, <10 IU/ml). Renal biopsy was planned but the patient refused the procedure. After 6 days of oliguric period, his clinical condition and renal functions returned almost to normal with supportive care within 12 days.

CONCLUSION: Malignant diseases may be a trigger for either the generation of some autoantibodies. Attention must be paid when interpreting the Anti-dsDNA positivity in malignant patients with AKI mimicking RPGN.

KEY WORDS: Kidney injury, Anti-dsDNA, Prostate cancer

ÖZ

AMAÇ: Maligniteye sahip hastalarda otoimmün ve romatolojik olaylar meydana gelebilmektedir. Bu özellikler; kombinasyon kemoterapilerinin kullanımından, tümor hücrelerinin eklem ve kasları direk tolarak invaze etmesinden, paraneoplastik sendromlardan, otoantikorlardan kaynaklanır. Bu vakada biz hızlı ilerleyen glomerülonefriti taklit eden akut böbrek yetmezlikli, prostat kanserli bir olguda görülen Anti-double-stranded deoxyribonucleic acid antibodies (Anti-dsDNA ab) pozitifliğini sunmayı amaçladık.

OLGU SUNUMU: 78 yaşında erkek hasta, 2 aydır yaygın kemik ağrısı, ani başlangıçlı zayıflama, 3 gündür ortaya çıkan dizüri, oligüri şikayetleri nedeniyle hastaneye yatırıldı. 2 yıldır metastatik prostat kanser tanısı mevcuttu. 5 gündür yaygın kemik ağrısından dolayı naproksen sodyum kullanmaktaydı. Serum kreatinin düzeyi hastaneye yatışında yüksek tespit edildi (2,4 mg/dl). Tam idrar tetkikinde; mikroskopik hematüri, 1,2 gr/gün proteinürisi mevcuttu. Anti-dsDNA pozitif idi (96 IU/ml [normal, <10 IU/ml]). Hasta reddettiği için renal biopsi yapılamadı. Oligürinin 6. gününden sonra renal fonksiyonlar normale dönmeye başladı.

SONUÇ: Malign hastalıklar bazı otoantikorların yapısında değişiklikler meydana getirebilir. Hızlı ilerleyen glomerülonefritli ve maligniteli hastalarda Anti-dsDNA pozitif olabilir.

ANAHTAR SÖZCÜKLER: Böbrek hasarı, Anti-dsDNA, Prostat kanseri

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INTRODUCTION

Anti-double stranded DNA antibodies (anti-dsDNA ab) have been identified in systemic lupus erythematosus (SLE) for more than 50 years. Many clinical correlations between their presence and disease activity have been demonstrated. On the other hand, patients with some diseases and disorders other than SLE may occasionally have test positivity for anti-dsDNA ab. We present a case with prostate cancer and acute kidney injury (AKI) mimicking rapidly progressive glomerulonephritis with a positive test for anti-dsDNA ab.

CASE REPORT

The 78-year-old male patient presented at our center with the complaint of generalized bone pain for approximately two months, and rapid onset of weakness, oliguria and dysuria for three days. He had been diagnosed with metastatic prostate cancer (PC) two years ago and at the time of presentation had received naproxen sodium because of severe bone pain for five days. On admission, pallor, crackles on lung bases, and edema were detected. Blood pressure was 140/85 mmHg. His laboratory data revealed a serum creatinine level of 2.4 mg/dl, albumin of 2.9 gr/dl, hemoglobin of 8.2 gr/dl and erythrocyte sedimentation rate of 102 mm/h. Leucocyte and platelet count, as well as serum levels of calcium, uric acid, fasting blood glucose, creatine kinase, liver transaminases, and serum and urine protein electrophoresis were normal. Urinalysis showed microscopic hematuria, granular casts and proteinuria of 1.2 gr/day. Both kidneys were assessed as normal on renal Doppler ultrasound. Naproxen sodium was stopped. As serum creatinine increased gradually to 3.5 mg/dl on the follow up, we considered RPGN, and therefore decided to perform immunologic tests. P- and c-antineutrophil cytoplasmic antibodies, anti-glomerular basement membrane antibody, rheumatoid factor and antinuclear antibody were negative, but anti-dsDNA ab was positive with a value of 96 IU/ml (normal, <10 IU/ml). Renal biopsy was planned but the patient refused this procedure. Diagnostic criteria for SLE were insufficient. On the following days, serum creatinine level reached a peak level of 6.7 mg/dl. Within twelve days after this peak, the subject's urine volume gradually increased to 3000 cc and serum creatinine level decreased to 1.6 mg/dl. Narcotic analgesics were administered for bone pain. After three months of follow-up, serum creatinine was 1.2 mg/dl, anti-dsDNA ab was still positive (88 IU/ml), and urinalysis revealed only microscopic hematuria. In our opinion, the patient's clinical diagnosis was acute tubular necrosis related to the non-steroidal anti-inflammatory drug.

DISCUSSION

Malignant diseases may be associated with the induction of autoimmunity that is characterised by the generation of autoantibodies against a wide range of autoantigens (1). Autoantibody activity (anti-oncoprotein antibodies, anti-tumor suppression genes, antiproliferation-associated antigens, antionconeural antibodies, etc.) has been identified in the serum of patients with solid tumors. Various paraneoplastic syndromes affecting the kidneys have also been reported. Some authors have reported a wide range of glomerular pathological changes and abnormal urinary sediments in these kind of patients. Membranous nephropathy, a clinical entity manifested by nephrotic syndrome, is highly associated with solid tumors (2). In our patient, there were symptoms and signs for acute nephritic syndrome but not for chronic glomerular disease.

Immunologic analysis including anti-dsDNA ab were performed in our patient because of acute nephritic syndrome and rapidly progressive glomerulonephritis. The anti-dsDNA ab level was elevated 9 fold but the criteria were inadequate for SLE diagnosis in our patient. Anti-dsDNA ab level was still high after 3 months of follow-up. Anti-dsDNA ab has also been found at low frequency (generally less than 5 percent), and usually in low titer in patients with rheumatoid arthritis, Sjögren's syndrome, scleroderma, Raynaud phenomenon, mixed connective tissue disease, discoid lupus, myositis, uveitis, juvenile arthritis, antiphospholipid syndrome, Grave's disease, Alzheimer disease, and autoimmune hepatitis (3). There were no signs or symptoms regarding these clinical conditions or diseases in our patient.

Anti-dsDNA abs are typically absent in drug-induced lupus, but can be positive in patients receiving minocycline, etanercept, infliximab and penicillamine. Along with the production of autoantibodies, these patients can develop a syndrome of arthritis/arthralgias, cutaneous vasculitis, and serositis (4). Our patient did not receive any medications other than naproxen sodium, and there were no vasculitic signs.

Positive anti-dsDNA ab tests in subjects without SLE was also found in some malignancies such as lymphoma, thymoma, lung, breast, stomach, and cervical cancer (5*)* In patients with PC, some autoantibodies (i.e., anti-neuronal antibody (6), anti-basement membrane zone autoantibodies to laminin (7), voltage-gated potassium channel autoantibodies (8), IgA type anticardiolipin antibody (9)) have been detected in patients' serum, but there are no reports of anti-dsDNA ab positivity in PC patients yet.

CONCLUSION

This is the first report of anti-dsDNA ab positivity in a patient with PC. The factor(s) that trigger the development of anti-dsDNA ab and the clinical importance in the human body is still unclear. One must be careful when interpreting anti-dsDNA positivity in patients with AKI mimicking RPGN who also have a malignancy. Epidemiologic and mechanistic studies are needed to determine the true prevalence of autoantibodies in prostate cancer and to investigate the importance of this issue.

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