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Case Report / Olgu Sunumu

Venlafaxine-Induced Hematuria and Prostatism: a Case Report

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ABSTRACT

Venlafaxine-induced hematuria and prostatism: a case report

Hematuria and prostatism are important medical conditions affecting the quality of life. They are most often seen causally related to prostate hyperplasia but may also occur as a side effect of certain medications. Although the urogenital side effects of antidepressants are common in the literature, reports that indicate antidepressant induced hematuria are rare. Venlafaxine, an antidepressant that inhibits serotonin-noradrenaline reuptake, is used in clinical practice in a number of psychiatric disorders, especially in major depressive disorder. Although it is a safe and effective antidepressant, it can cause side effects. We present a 55-year-old man with hematuria and symptoms of prostatism starting after the use of venlafaxine that resolved after the withdrawal of venlafaxine. In the literature, symptoms of prostatism have been reported related to antidepressants that are effective through the noradrenaline mechanism, such as venlafaxine, duloxetine, milnacipran, and reboxetine, but there are no reports on hematuria. As far as we know, this is the first report to present a case of venlafaxine-induced hematuria.

Keywords: Antidepressants, hematuria, prostatism, venlafaxine

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ÖZ

Venlafaksin kaynaklı hematüri ve prostatizm: Bir olgu sunumu

Hematüri ve prostatizm yaşam kalitesini etkileyen önemli bir tıbbi durumdur. En sık prostat hiperplazisi nedeni ile görülüyor olsa da bazı ilaçların yan etkisi olarak da görülebilmektedir. Literatürde antidepresanların ürogenital yan etkileri sık görülmesine rağmen hematüriye neden olduğuna dair raporlar nadir görülmektedir. Venlafaksin klinik pratikte majör depresif bozukluk başta olma üzere çok sayıda psikiyatrik bozuklukta kullanılan serotonin-noradrenalin geri alım inhibitörü bir antidepresandır. Güvenli ve etkili bir antidepresan olmasına rağmen bazı yan etkileri de bilinmektedir. Olgumuzda venlafaksin kullanımı sonrası hematüri ve prostatizm semptomları başlayan ve venlafaksin kesilmesi sonrası şikayetleri sonlanan 55 yaşında erkek hasta sunuyoruz. Literatürde venlafaksin, duloksetin, milnasipran ve reboksetin gibi noradrenalin mekanizması üzerinden etkili antidepresanlara bağlı prostatizm semptomları rapor edilmiş olsa da hematüri ile ilgili bir rapor bulunmamaktadır. Bildiğimiz kadarıyla vakamız venlafaksin kaynaklı hematüri olgusunun sunulduğu ilk rapordur.

Anahtar kelimeler: Antidepresan, hematüri, prostatizm, venlafaksin

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INTRODUCTION

Prostatism is a medical condition with clinical and social repercussions diminishing the quality of life. While its most common cause is prostate hyperplasia, it is a condition occurring in relation to any obstruction of the urethra or an increased pressure in the urinary tract. First symptoms are poor urinary flow and straining to void, problems in urine projection, hesitancy before starting to urinate, post-micturition dribble, and the feeling of incomplete bladder emptying (1,2). While less severe cases may be tolerated, in severe states microscopic or macroscopic hematuria can be found in the urine (3). As well as being disease-related, this uncomfortable situation may also be seen as a side effect of the use of opiates or drugs such as α-adrenergic agonists (4).

Venlafaxine is a strong serotonin and noradrenaline receptor antagonist and a weak dopamine receptor antagonist, frequently used in clinical practice as an antidepressant in the treatment of a number of mental conditions such as major depressive disorder or anxiety disorder (5). The strongest dose-related effect is serotonergic, then noradrenergic, and in high doses, the drug also has a dopaminergic effect. Being an effective and well tolerated antidepressant, venlafaxine has a

comparatively low profile of side effects, which, as well as its effectiveness, depends on the dose (6). Most commonly seen adverse effects are nausea, vomiting, reduced appetite, diarrhea, dryness of the mouth, constipation, drowsiness, and changes in the liver enzymes (7). Side effects in the urinary system are much rarer. There are case reports in the literature regarding urinary incontinence caused by venlafaxine (8,9). While our literature review identified one case with prostatism (10), we found no reports regarding hematuria.

This case report presents a 55-year-old male patient with prostatism symptoms after venlafaxine use developing hematuria.

CASE

A 55-year-old married male, employed as a worker, presented to our psychiatry clinic complaining of anhedonia, lack of appetite, unhappiness, acedia, and lack of energy. After a detailed anamnesis and mental examination applying DSM-5 criteria, the patient, who did not have a previous psychiatric history, was diagnosed with major depressive disorder. He was started on venlafaxine 75mg/day, which was titrated over 2 weeks up to 150mg/day. The patient scored 46 on the Hamilton Depression Scale and 29 on the Hamilton Anxiety Scale. Three weeks after starting the venlafaxine dose of 150mg/day, the patient came in for a control examination; because of blood found in the urine, frequent micturition, and need to strain while urinating, a urological consultation was requested. The etiological workup for the patient, who did not have any disease and was not on any medication, included blood (full blood, urea, creatinine, prostate-specific antigen, sedimentation, CRP) and urine examination (full urine), urological examination (assessed by detailed anamnesis, examination, laboratory diagnostics, and uroflowmetry), and imaging examinations (ultrasonography, tomography); no results explaining the symptoms were obtained. Consultations in internal medicine and nephrology showed the patient's renal functions to be normal. Given the temporal correlation between onset of symptoms and starting of venlafaxine use, it was decided to stop the administration of venlafaxine. The patient was started on sertraline 50mg/day. His complaints gradually decreased over the course of two weeks and then disappeared. Upon follow-up, the urological complaints did not recur. Using the Naranjo Adverse Drug Reaction Probability Scale, it was found that venlafaxine-related prostatism and hematuria are "likely drug-related side effects" (Naranjo adverse drug reaction score=6) (11).

DISCUSSION

Psychiatric disorders are frequently seen. In clinical practice, serotonin-noradrenaline reuptake inhibitors (SNRIs) are often chosen for the treatment of these diseases as they have a low profile of adverse drug reactions. To our knowledge, there are no cases in the literature reporting hematuria related with venlafaxine use. However, prostatism has been reported in relation with the use of venlafaxine (10) and milnacipran (12). There are also reports about duloxetine (13) and reboxetine (14) causing similar symptoms. All of these drugs are characterized by noradrenaline reuptake inhibiting properties. In our case, after the use of venlafaxine hematuria and prostatism symptoms started. To our knowledge, our case is the first of its kind to be reported.

It is known that serotonin and noradrenaline play an important role in the organization of the lower urinary system (15). The pudendal somatic motor nucleus of the spinal cord is densely innervated with serotonin (5HT) and noradrenaline terminals. In the light of this information, given that prostatism is seen with agents acting on noradrenaline, such as venlafaxine and milnacipran, but not with serotonin reuptake inhibitors, we may assume that the probable mechanism of this adverse effect could also cause an increase in the extracellular concentration of noradrenaline due to the activation mechanism of venlafaxine in subtypes of the adrenergic receptors (16). Based on this hypothesis, in our case we chose an antidepressant from the SSRI group after the development of adverse effects with venlafaxine.

Normally, a very small number of erythrocytes can be found in the urine unrelated to any particular reason (17). If the erythrocyte number is greater than expected, we can talk about hematuria. Macroscopic (red or brown urine, visible to the naked eye) or microscopic hematuria can occur related to very different causes, either as an isolated symptom or as one of a range of symptoms. While our patient presented with a complaint of hematuria, tolerable prostatism symptoms were also present.

Related to the degree of their serotonin uptake inhibition, antidepressants might affect the serotonin uptake mechanism in the platelets and thus interfere with hemostasis (18). Studies supporting this hypothesis suggest that antidepressants reduce intraplatelet serotonin contents, affect platelet aggregation, and prolong closing time (19). From this perspective, we can assume that the hematuria seen in our case stemmed from the serotonin reuptake inhibition effect of venlafaxine. However, we should not forget the possibility that the hematuria might have been a secondary hemorrhage caused by the physical effects of the symptoms of prostatism.

Side effects of drugs can be assessed with the adverse drug reaction probability scale developed by Naranjo et al. (11) The score ranges between 0 and 13 points, whereby 9 points and above means the effect is "definite," between 5 and 8 points "probable," between 1 and 4 points "possible," and at 0 points "doubtful." In the assessment according to this scale, our case scored a total of 6 points: 1 point for previous publication reporting hematuria and prostatism related to venlafaxine use, 2 points for onset of hematuria and prostatism after administration of the suspected drug, 1 point for disappearance of side effects after discontinuing the drug, and 2 points for the absence of other detectable possible reasons for hematuria and prostatism. This data suggests that the adverse effect is probably related to venlafaxine.

There are some limitations in this report. In our patient, venlafaxine plasma level determination and cysto-ureteroscopic studies were not done. In addition, these examinations would not have been practical, given that the patient's complaints resolved after the change of antidepressant.

In conclusion, the presence of hematuria and prostatism symptoms seriously affects the quality of life and social relations. Venlafaxine-related prostatism symptoms are relatively rare and are often tolerable for the patient. However, as no risk factors for venlafaxine-induced hematuria and prostatism are known, clinicians should be careful when prescribing antidepressants acting through noradrenaline mechanisms, particularly venlafaxine. The number of studies reporting effects of venlafaxine use on the urogenital system is limited. In order to illuminate the mechanism of hematuria and prostatism symptoms related to the use of venlafaxine, controlled studies with larger samples are required.

Contribution Categories		**Author Initials**
Category 1	Concept/Design	I.G.
	Literature review	I.G., A.K.
	Data analysis/Interpretation	A.K., A.A.
	Case follow-up (if applicable)	I.G., A.K., A.A.
Category 2	Drafting manuscript	I.G.
	Critical revision of manuscript	A.A., A.K.
Category 3	Final approval and accountability	I.G., A.K., A.A.
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