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### CASE REPORT

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## Brain-bladder axis: a case of anxiety-associated haematuria

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#### **ABSTRACT**

Focusing on the interface between psychiatry and medicine, psychosomatic medicine has become a subspecialty of psychiatry. A psychosomatic medicine psychiatrist is like a medicalpsychiatric detective, discovering the clues to psychosomatic patients, and improving their psychiatric care. However, underdiagnosis of psychosomatic disorders is not uncommon. This is because psychosomatic symptoms are usually nonspecific and can come in different disguises, leading physicians to overlook them initially. As a psychosomatic medicine psychiatrist, being familiar with the various ways psychosomatic disorders can present is particularly important in clinical practice. Here, we report a patient who developed haematuria that was later considered an underdiagnosed psychosomatic symptom. A 24year-old man developed significant anxious and depressive symptoms. Meanwhile, he experienced gross and microscopic haematuria. Urinalysis showed cloudy urine with 50/µL occult blood, 116 red cells, and 2 white cells per high-power field, and no proteinuria or casts. Abdominal and pelvic sonography and intravenous urography did not reveal any significant finding. Cystoscopic examination revealed an increased contraction of the muscle wall without stricture or cystitis of the bladder. Cytologic evaluation of the urine showed no malignant cells. After four sessions of psychotherapy, the patient admitted that his worsening anxiety was mainly related to the issue of him being a homophobic gay, and his homophobia clearly accentuated his anxiety. In the following psychotherapy, he was better able to discuss his ideas about gay men. Interestingly, the patient's haematuria gradually resolved. Because of the relief from his internal discomfort with homosexuality, the psychotropic drugs were gradually discontinued. During the 12 months of follow-up, the patient never had a recurrence of microscopic and macroscopic haematuria. We suggest that the patient's haematuria resulted from the remarkable anxiety symptoms because the haematuria occurred during his development of severe anxiety symptoms, and it improved as the anxiety symptoms were relieved. We discuss the possible mechanisms and suggest a "brain-bladder axis." The breakdown of the mucosal protective defences is a potential mechanism linking anxiety to haematuria. Besides, neurons or microglia synthesize prostaglandin in response to physiological or psychological stress, and prostaglandin E2 is one of the factors generated in this scenario. This case provides another clue to idiopathic haematuria and suggests the possibility of underdiagnosis of psychiatric disorders in cases of urologic conditions. We believe a better understanding of the complex interactions between the brain and the genitourinary system can help urologists and psychosomatic psychiatrists to improve treatments for patients with both conditions.

#### **ARTICLE HISTORY**

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#### **KEYWORDS**

Bladder; anxiety; haematuria; genitourinary system

#### Introduction

The increasing understanding of the neural basis of mental symptoms has rendered mind-body dualism theoretically untenable. Symptoms, be they physical or psychiatric, could be considered products of the interconnection of bodily, mental, and environmental problems. Focusing on the interface between psychiatry and medicine, psychosomatic medicine has become a subspecialty of psychiatry. The major groups of patients in the field of psychosomatic medicine are those with somatoform disorders, those with comorbid psychiatric and general medical conditions complicating each other's management, and those with psychiatric disorders resulting from the direct consequence of a medical condition or its treatment. In this vein, a psychosomatic medicine psychiatrist is like a medical-psychiatric detective, discovering the clues to psychosomatic patients, and improving their care.

Underdiagnosis of psychosomatic disorders is not uncommon. This is because psychosomatic symptoms are usually nonspecific and can come in different disguises, leading physicians to overlook them initially. Being familiar with the various ways psychosomatic disorders can present is particularly important in clinical practice. Here, we report a case in which haematuria was associated with clinically relevant anxiety and depression. To our knowledge, haematuria has not yet been linked to psychosomatic problems.

#### **Case report**

A 24-year-old man presented at our clinic with a chief complaint of anxiety and depression. In the past 5 years, he had experienced two severe episodes, which required antidepressant and anxiolytic treatment. However, after the resolution of the symptoms, he stopped his regular visits and didn't take any psychotropic drugs. Around six months ago, he experienced another episode, demonstrating depression, anxiety, profound insomnia, muscle tension, and inability to concentrate. Meanwhile, intermittent gross haematuria and urinary frequency occurred.

A detailed history taking revealed that the patient had been physically healthy, and denied cigarette smoking, alcohol assumption, illicit drug use, and specific occupational exposures. He also reported that he was sexually inactive and his family history was negative for any serious disorders.

The patient appeared well, and the physical examination, involving genitalia, did not reveal any abnormality. Blood test results, including the platelet count, tests of coagulation, and renal function were normal. A test for human immunodeficiency virus showed negative results. Urine drug screens did not reveal anything of note. Urinalysis showed cloudy urine with 50/µL occult blood, 116 red cells, and 2 white cells per high-power field, and no proteinuria or casts. Abdominal sonography and intravenous urography did not reveal any significant finding. Cystoscopy revealed an increased contraction of the muscle wall without stricture or cystitis. Urinary cytologic showed no malignant cells.

Because of the remarkable anxiety symptoms, bupropion 150 mg/d and alprazolam 1 mg/d were started. However, over the subsequent two months, he did not respond to these psychotropic drugs, and intermittent haematuria persisted. A biweekly psychotherapy session was then started, which gradually improved his adaptation to the problematic thought and helped him to learn relaxation. After four sessions, the patient admitted that his worsening anxiety was mainly related to the issue of him being homosexual. Moreover, he expressed as a homophobic gay, and his homophobia clearly accentuated his anxiety symptoms. In the following sessions of psychotherapy, he was better able to discuss his ideas about gay men and did not believe that he was a socially stigmatized person. Interestingly, the patient's haematuria gradually resolved, and urinalysis demonstrated no significant finding. Because of the relief from his internal discomfort with homosexuality, the psychotropic drugs were gradually discontinued. During the 12-month follow-up, the patient never had a recurrence of haematuria.

## **Discussion**

We strongly believe that the patient's haematuria resulted from anxiety because the haematuria

occurred during his development of severe anxiety symptoms, and it improved as the anxiety symptoms were relieved. Although the cystoscopy showed an increased contraction of the muscle wall, a diagnosis of overactive bladder is unlikely. This is because the patient did not show the typical symptoms of overactive bladder, that are urgency, nocturia, and incontinence; moreover, haematuria is an important criterion by which to exclude the diagnosis of overactive bladder syndrome [1].

We suggest that the breakdown of the mucosal protective defences is a potential mechanism linking anxiety to haematuria. As an adaptation to stress, the blood is shunted away from the viscera and skin, thereby preserving perfusion to the vital organs. In short-term stress, the temporary shunting of visceral blood flow can be well tolerated; however, if the emotional storm the patient suffers continues for a long period of time, the resultant hypoperfusion may cause mucosal ischemia. Importantly, chronic bladder ischemia can promote the release of leukotriene and prostaglandin in the bladder wall [2], thereby leading to inflammation or even to ulcerative lesions in the bladder. Besides, chronic ischemia can cause bladder hyperactivity through sensitization of afferent pathways, activated by tachykinin-containing nerves and neurokinin receptors [3]. This concurs with the patient's findings on cystoscopic examination.

Additionally, neurons or microglia synthesize prostaglandin in response to physiological or psychological stress, and prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) is one of the factors generated in this scenario. In the genitourinary system, PGE2 can enhance the micturition reflex and facilitate afferent nerve activity [4]. Animal evidence shows that repeated stress may increase PGE<sub>2</sub> in mice [5]. Moreover, it is suggested that PGE2 increases voiding contraction amplitude and triggers micturition [6]. The repeated muscle spasm may occur as a consequence of psychological stress, leading to hypoperfusion, ischemia, and even mucosal bleeding.

The common causes of haematuria include infections, stones, benign prostatic hyperplasia, glomerulonephritis, trauma, cancer, and prostatitis. However, in up to 43-68% of the cases of haematuria the aetiology is unknown [7]. Based on available evidence and the observations from our patients, the "brain-bladder axis" is a heuristic concept to describe the association between urologic conditions and psychiatric disorders. Our case provides another clue to idiopathic haematuria and suggests the possibility of underdiagnosis of psychiatric disorders in cases of urologic conditions. Interestingly, most people can experience changes in voiding function in response to increased anxiety and stress, but neither urologists nor psychosomatic psychiatrists are familiar with the concept of "brain-bladder axis." Undoubtedly, a better understanding of the complex interactions between the brain and the



genitourinary system can help us to improve treatments for patients with both conditions.

#### **Disclosure statement**

No potential conflict of interest was reported by the authors.

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